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THE QUALITATIVE ANALYSIS OF MEDICINAL PREPARATIONS

BY

H. C. FULLER, B.S.

In Charge of Division of Drug and Food Products,
Institute of Industrial Research,
[illegible]

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PREFACE TO SECOND EDITION

THIS work was published with the hope that it would prove to be of as much assistance to other workers in the field of drug chemistry as it had been to the author and his co-workers.

The correspondence received by the author since its publication has fully justified the expectations.

In revising the work the general plan of the first edition has been retained. The scheme of separation has been elaborated in order to facilitate the identification of the substances removed by immiscible solvents from an acid solution, and procedures have been given for separating the alkaloids which are commonly found together in mixtures. A complete scheme for the identification of metals and inorganic acids has been added, and a method for identifying volatile oils proposed by Nelson has been included in the chapter on Liniments.

Few changes have been made in the second portion of the work. The directions originally proposed have stood the test of many years of experimental work, and except for an amplification of the procedure for examining emulsions and for identifying the volatile constituents of liniments and the addition of a section on Chewing Gums, that portion of the book remains practically as it was in the first edition.

INTRODUCTION

DURING recent years the analysis of medicinal preparations has become very important, and there have been evolved many new methods for determining the active ingredients contained therein, as well as new reactions for the identification of different substances. In the latter case, the tests almost invariably apply to the substances in question when they are alone and in the pure condition, and take no account of the influence which might be exerted on the reaction if other things were present, a condition usually obtaining in attempting to identify the constituents of a complex medicine. Before one can, with any degree of certainty, proceed with the quantitative analysis, it is necessary to know the character of the components, and, up to the time this book was originally published there was no systematic scheme for obtaining this information. The Dragendorff and Stass-Otto methods of separation are satisfactory so far as they go, but they fall short of giving a complete analysis or separation of the manifold substances with which one has to deal when analyzing drug products.

From the analysis of several hundred mixtures, a scheme of separation has been gradually evolved by which the different substances are obtained at certain stages of the manipulation, and their identity established with a few readily applied tests. A knowledge of the use to which a particular preparation is to be employed is

often a guide in arriving at conclusions as to its composition, and its price will often suggest what might *not* be present; in fact, a drug analyst can, with advantage, be more than a chemist pure and simple—he should familiarize himself with the uses of the ordinary drugs, and have some idea of the current market conditions.

It is not the intention of this work to describe in detail the chemical and physical properties of the substances involved; as such data are available, it would be superfluous to repeat them here, and the laboratory should contain for ready reference, the following works: "U. S. Pharmacopœia;" "U. S. and National Dispensatories;" "The Vegetable Alkaloids," Pictet and Biddle; "Plant Principles," Sohn; "Die Pflanzen Alkaloide," Bruhl, Hjelt and Aschan; "Die Glucoside," Van Rijn; "The Volatile Oils," Gildemeister and Hoffman; "Newer Remedies," Coblentz; Merck's Index; "Manual of Chemical Analysis," Newth; "Detection of Poisons," Autenreith; "New and Non-Official Remedies," American Medical Association; "The Identification of Organic Substances," Mulliken.

The work is divided in the following manner: The first portion describes the preliminary manipulation which separates the ingredients into large groups, then the scheme for separating these into smaller groups and individuals, and the tests for their identification; the second portion describes the methods to be employed in manipulating the various classes of medicinal products to make them available to separation in accordance with this scheme.

A diagrammatic arrangement, showing the essentials of the scheme at a glance follows:

CONTENTS

THE QUALITATIVE ANALYSIS *of* MEDICINAL PREPARATIONS

FIRST PORTION

Scheme of Analysis for the Separation and Detection of Substances in Medicinal Products

If the sample is a liquid, note the odor, which will indicate the presence of volatile oils, ammonia, phenols, etc. Transfer the sample to the flask of a distilling apparatus, dilute with an equal volume of water, and distill carefully until a volume of liquid about equal to that of the sample taken has passed over. Reserve the liquid in the distilling flask and designate it as Liquid I. Note the reaction of the distillate to litmus; if the sample was acid or neutral in the beginning and now has an alkaline reaction, the presence of ammonium salts and strong alkaloids in the liquid left in the distilling flask is indicated.

Test for Formaldehyde.—Transfer a portion of the distillate to a small beaker, and if alkaline, render acid with sulphuric acid. Warm on steam-bath and note odor of vapors, which will have the characteristic smell and sensation of formaldehyde if this substance is present. Remove from bath and invert over the beaker an evaporating dish smeared with concentrated sulphuric acid con-

taining dissolved morphin. A purple color will quickly develop if formaldehyde is present.

Test for Phosphorus.—Test a portion of the distillate with an equal volume of chlorine water, stopper, and let stand several hours or overnight. Transfer to a beaker, dilute with water, boil off excess of chlorine, cool, neutralize with ammonia, then add an excess of nitric acid, followed by ammonium molybdate, and warm. The appearance of the canary-yellow ammonio-phosphomolybdate indicates the presence of phosphorus.

If hypophosphorus acid is present, the same reaction may occur, hence, before oxidizing, the distillate should be tested with litmus, and if found acid, it should be neutralized with calcium carbonate and redistilled.

Iodin.—If the distillate is brownish or yellowish, dilute a portion, add a few c.c. of carbon bisulphide and agitate, noting any color imparted; iodin dissolves in the bisulphide, imparting to it a violet to purple color. Another portion of the distillate is diluted and treated with a few drops of starch paste; on shaking, the entire liquid will become deep blue if iodin is present, and on warming the color will disappear, coming back again on cooling.

Test for Alcohols, Acetone and Chloroform.—If volatile oils and chloroform are indicated, transfer the distillate to a separator, add sodium chloride crystals to saturation (if iodin is present decolorize with sodium sulphite), add low-boiling petroleum ether and agitate thoroughly. After settling, draw off the aqueous layer and repeat. Then run the aqueous layer into a distilling flask and distill until the volume is reduced about one-half.

To a portion of the distillate add a few crystals of sodium acetate, followed by 1 to 2 c.c. of concentrated sul-

phuric acid and heat just to boiling. If ethyl alcohol is present the pleasant fruity odor of ethyl acetate is given off.

To a portion of the distillate add a few drops of iodin solution, followed by a slight excess of sodium hydroxide. If iodoform is obtained and precipitates within a few moments in the cold, acetone is indicated. Ethyl alcohol yields a precipitate of iodoform in the cold on standing fifteen to thirty minutes, and immediately on warming to 70°.

To 2 to 3 cc. of the distillate add 2 to 3 drops of 1 per cent sodium nitroprusside and then 2 to 3 drops of 10 per cent sodium hydroxide. Divide into two portions, *a* and *b*. To *b* add 3 to 5 drops glacial acetic acid. In the presence of as much as 1 to 2 per cent of acetone, *a* is at first orange or yellowish-orange, changing after twenty minutes to a clear yellow; *b* is as first red when viewed against a white background, the hue being unchanged after twenty minutes, although the intensity decreases so that in the case of solutions containing as little as 1 per cent of acetone the color is so pale as to be barely distinguishable.

To 10 c.c. of the distillate add 1 gram solid potassium hydroxide, and without waiting for it to dissolve add 10 drops salicylaldehyde and warm to 70°. In the presence of acetone a purple-red contact ring develops; or if the hydroxide is all dissolved before the addition of the salicylaldehyde, the liquid becomes yellow, then reddish- and finally purplish red.

One c.c. of the distillate is placed in a small round-bottom distilling flask, 0.8 gram ammonium persulphate and 3 c.c. dilute sulphuric acid (1.5), or 1.5 grams potas-

sium bichromate and 1.5 c.c. concentrated sulphuric acid, followed by 20 c.c. water. Distillation is then conducted collecting 1 c.c. fractions in separate test-tubes. To the distillate add a few grains of morphin and when dissolved introduce sulphuric acid by means of a pipette so as to form a layer at the bottom of the tube. If formaldehyde is present, due to oxidation of methyl alcohol, a violet ring will be formed at the junction of the two liquids.

The petroleum ether solutions used for removing the volatile oils and chloroform are mixed and divided into two portions. Distill off the bulk of the petroleum ether from one portion, add a few crystals of acetanilid, followed by 5 to 10 c.c. of potassium hydroxide, agitate, then warm, then agitate vigorously, and note whether any isonitrile is evolved. To the other portion add an equal volume of alcoholic alkali and boil under a reflux for half an hour. Evaporate the solvent, dissolve residue in water, add excess of nitric acid, filter if necessary, and add silver chloride nitrate to the filtrate and note any precipitate, of silver chloride, potassium chloride being produced by saponification of chloroform.

NOTE.—If formaldehyde is present, it must be removed before testing for alcohols. Treat the distillate to be tested with an excess of meta phenylene-diamine hydrochloride, which will form an insoluble precipitate with formaldehyde. Redistill and examine distillate as above described.

Hydrogen Peroxide.—Some liquid preparations may contain hydrogen peroxide. If volatile substances other than water are present, evaporate over the steam-bath to a fairly concentrated solution, dilute with water, if

acid in reaction, neutralize with dilute alkali, and again make acid with dilute sulphuric acid, filtering from any precipitate that may have formed.

Pour a few c.c. of the solution into a small separator, add 5 c.c. absolute ether, 1 to 2 c.c. of potassium chromate, and if the liquid is not acid, 1 to 2 drops of dilute sulphuric acid. In the presence of peroxide a blue color appears which will dissolve in the ether when the separator is agitated.

Treat a few c.c. of the solution with a solution of titanium sulphate, followed by a little dilute sulphuric acid (if not already acid). A yellow color is produced, depending on the quantity of peroxide.

The liquid I in the distilling flask is evaporated until all water is driven off. It is then treated with 95 per cent alcohol as described below:

If the substance is a solid it is ground up in a mortar and treated with alcohol, 95 per cent, stirring thoroughly, warming if necessary to get the material into solution, decanting the filtered liquid if any remains undissolved. Repeat several times, if necessary.

(*a*) Substances soluble in alcohol. Evaporate and treat the residue with water, filtering into a flask. Set aside one-third of the aqueous solution A, then treat the solution with dilute acid.

(1) Substances soluble in water. Treat according to the scheme of separation described on page 10.

(2) Substances insoluble in water. Treat as described on page 93.

(*b*) Substances insoluble in alcohol. Treat with water and filter.

(3) Substances soluble in water. Treat as described on page 102.

(4) Substances insoluble in water. Treat as described on page 105.

By the above process the substances mentioned below will have separated approximately into the respective groups:

(1) Substances Soluble in Water

Ammonium acetate
Ammonium carbonate
Calcium bromide
Calcium chloride
Gold chloride
Iron chloride
Mercuric chloride
Mercuric cyanide
Lithium bromide
Potassium bromide
Potassium thiosulphate
Potassium iodide
Potassium nitrate (very slightly sol. alcohol)
Potassium permanganate, decomposed by alcohol
Silver nitrate
Sodium acetate
Sodium arsenate
Sodium bisulphate
Sodium bromide
Sodium chlorate
Sodium thiosulphate
Sodium iodide
Sodium nitrate
Sodium nitrite, slightly sol. alcohol
Sodium sulphite, spar. sol. alcohol
Strontium bromide
Strontium iodide
Zinc chloride
Zinc bromide
Zinc iodide
Iron and quinin citrate
Iron and strychnin citrate
Lead acetate (somewhat sol. in alcohol)
Lithium benzoate
Lithium salicylate
Potassium citrate (spar. sol. in alcohol)
Soap
Sodium benzoate
Sodium glycerophosphate (very slightly sol. in alcohol)
Sodium salicylate
Sodium sulphocarbolate
Zinc valerate
Chloral hydrate
Guaiacol phosphate
Sublamine

Acetanilid (moderately sol. in H_2O)
Acetozone
Acetphenetidin (slightly sol. in water)
Adrenalin (sol. acids)
Alphozone
Acid salicylic
Acid benzoic
Acid citric
Acid tartaric

Antipyrin
Apiin
Aristochin (sol. acids)
Asaprol
Benzacetin (Acetamido-methyl-salicylic acid)
Benzoiin (Phenylbenzoyl-carbinol-bitter almond-oil camphor)
Bromural
Catechu
Chinaphenin (sol. acids)
Chloretone
Chrysarobin (partly soluble in water, dissolves readily in alkalies)
Chrysophanic acid (slightly sol. in alcohol and water—dissolves readily in alkalies)
Convallamarin
Coriamyrtin
Coryfin
Cyclamin
Epicarin (somewhat sol. in water)
Emodin (sol. alkaline sol.)
Ergotinin
Esculin
Eucalyptus gum—Red gum
Eugenoform (diff. sol. alcohol)
Euphorin (sol. in acids.)
Euphthalmin (sol. in acids)
Euquinin (sol. in acids)
Formanilid
Formicin
Gallanol
Gallicin
Gallobromal
Galloformin (diff. sol. in both water and alcohol)
Gamboge (partly sol. in alcohol and water)
Glycerin
Glycosal
Guaiamar
Hedonal
Ichthyol comps. (acids pptng. ichthyol)
Isopral
Kino
Lysidin
Manna (from alcohol deposits mannitol on cooling)
Mesotan
Musk (partly)
Myrrh (partly)
Neuronal
Novaspirin
Novocain base (sol. acids.)
Orthoform
Oxaphor
Oxgall, purified
Periplocin
Phloridzin
Resorcinol
Resorcylalgin
Salophen
Spirosal
Sucrose (Sugar) (dissolves somewhat in alcohol)
Sulphonal
Tannosal
Terpin hydrate
Tetronal
Thiocol (sl. sol. in alcohol)
Thiosinamin
Trional
Trioxymethylene
Urethane
Valyl
Veronal

(2) SOLUBLE IN ALCOHOL AND INSOLUBLE IN WATER

(E denotes the substances which may subsequently be removed by ether.)

Mercuric iodide (E)
Phosphorus (E)
Sulphur sublimed (E)
Iodin
Difluorodiphenyl (E)
Diiodoform
Ethyl diiodosalicylate (slightly sol. in water)
Ethyl iodide
Europhen
Iodoform (E)
Iodoformal
Iodonaphthol
Iron valerate (water decomposes it on boiling)
Nosophen (Tetraiodophenolphthalein—iodophenin) (E)
Orphol
Sanoform (E)
Terpene hydrochloride
Thymol iodide (E)
Tribromphenol (E)
Tribromsalol (E)
Trichlorphenol (E)
Acids—Glycyrrhizinic, Cerotic, Oleic, Palmitic, Stearic—Benzoic, Salicylic—(dissolve to some extent in water)
Alantol (E)
Ammoniac (part sol. water; pt. E)
Amyl nitrite (almost insol. in water)
Anemonin (sol. in $CHCl_3$)
Apiol (E)
Arhovin (E)
Asafetida (milky emulsion with water)
Balsam Peru (E, partly)
Balsam Tolu (E, partly)
Benzoin
Benzyl cinnamate—Cinnamein
Benzosol—Guaiacol benzoate (E)
Betanaphthol salicylate (E)
Burgundy Pitch (E)
Brometone (E)
Bromoform (E)
Camphor monobromated (almost insol. in water) (E)
Cannabinon
Chlorophyll (E)
Chrysarobin (E)
Cantharidin
Cinnamyl cinnamate (Styracin)
Cocain carbolate
Colophony (E)
Convallarin
Copaiba (E)
Creosote carbonate (E)
Cresalol (Cresol salicylate, E)
Damiana resin (E)
Eriodictyon resin (Yerba santa)
Eupyrin (E)
Filmaron (difficul. sol. alcohol, E)
Fluorescein
Fortoin (spar. sol. alcoh. and sol. alkalies, E)
Formopyrin (almost insol. alcoh.)
Formylphenetidin (sol. in hot water; E)
Galbanum (emulsifies with water; E)
Gallogen (soluble in alkaline liquids)
Grindelia robusta resin (E)

Gamboge (part. sol. alcohol; E)
Guaethol—Guaiacol ethyl
Guaiac (E,) partly)
Guaiacol carbonate—Duotal (E)
Guaiacol salicylate (E)
Homoeriodictyol (E) on shaking ether solution with Na_2CO_3 separates as Na salt
Hop resin (E)
Hypnoacetin
Iatrol
Iothion (E)
Kamala (part. sol. alcohol; E)
Kamalin
Kosin
Losophen
Mastic (E)
Methylene diguaiacol—Geoform
Monotal
Naphthalene (E)
α and β Naphthol (sparingly sol. in water; E)
Paraffin (E)
Phenolphthalein (E)
Protosal (E)
Resin jalap (E partly)
Resin podophyllum
Resin scammony (E)
Salitannol
Sapogenin
Salit (E)
Salol (very slight sol. in water; E)
Santonin (very slight sol. in water; E)
Salacetol (very slight sol. in water; E)
Storax (E partly)
Styracol—Guaiacol cinnamate
Sulphaminol
Styrene—Phenylethylene (E)
Tar (E)
Tannoform
Taraxacum resin
Tannopin
Triphenin
Turpentine (E)
Validol—Menthol valerate (oil; E)
Valerydin—Sedatin
Wax
Yerba Santa resin

(3) Insoluble in Alcohol but Soluble in Water

Arsenous acid
Aluminum and potassium-sulphate
Ammonium bicarbonate
Ammonium chloride (sl. sol. alcohol)
Ammonium phosphate
Antimony and potassium tartate
Calcium hypophosphite
Calcium thiosulphate
Iron pyrophosphate
Lithium carbonate
Magnesium sulphate
Potassium carbonate
Potassium nitrate
Sodium bicarbonate
Sodium biborate
Sodium carbonate
Sodium chloride (sl. sol. alcohol)
Sodium hypophosphite
Sodium phosphate
Sodium pyrophosphate
Sodium sulphate
Zinc sulphate

Calcium glycerophosphate
Enesol (Mercury salicylarsenate)

Ferrostyptin (insol. cold alcohol)
Iron citrate
Iron and ammonium citrate
Iron and ammonium tartrate
Iron and potassium tartrate
Lithium glycerophosphate
Lithium citrate
Mercurol
Potassium glycerophosphate
Potassium bitartrate (sparingly in alcohol)
Potassium and sodium tartrate
Sodium glycerophosphate
Acacia
Citarin
Creatin
Mannitol
Paraformaldehyde
Papain
Pancreatin
Pepsin
Quininphytin (Quinin anhydro-oxymethylenediphosphate)
Saloquinin (sol. acids)
Sulphanilic acid
Thiocol

(4) Insoluble in Alcohol and Water

Ammoniated mercury
Bismuth subcarbonate
Bismuth subnitrate
Calcium fluoride
Carbon
Cerium oxalate
Iron carbonate
Iron phosphate precipitated
Iron reduced
Magnesium carbonate
Magnesium oxide
Mercurous iodide
Mercurous oxide
Mercuric oxide (very sl. sol. in water)
Mercurous chloride
Sulphur precipitated
Zinc carbonate
Zinc oxide
Zinc phosphide
Airol (Bismuth beta-oxyiodogallate)
Bismuth citrate
Bismuth subgallate
Crurin (Quinolin-bismuth sulphocyanate)
Cutal (Aluminum borotannate)
Dermol (Bismuth chrysophanate)
Ferratin
Iodalbin (almost insoluble)
Iodol
Sajodin (Calcium iodobehenate)
Triferrin (Iron paranucleinate)
Cantharidin (sol. hot alcohol; but deposits on cooling)
Lard
Starch
Spermaceti (sol. in hot alcohol; but deposits on cooling)
Tannalbin (sol. in alkalies)
Xeroform

Now proceed with the examination of Solution A according to the following scheme of separation. It will be noted that the tables which follow include some of the

substances which were reported as being insoluble in water, but as the scheme is adapted to the procedures for examining the different classes of galenical products, the manipulation of which is detailed in the second section of the work, it is necessary to make provision for their occurrence.

Add dilute sulphuric acid and note any precipitate which may indicate glycyrrhizin and soap acids. Glycyrrhizin soon agglomerates and sticks to the sides of the container. The liquid should be decanted and the sticky precipitate washed with ice water. Dissolve in dilute ammonia and evaporate over the steam-bath. Ammoniated glycyrrhizin will dissolve in water, yielding a very sweet solution.

Acid Solution

Note whether the solution is fluorescent.

Pichi, pink fluorescence with acids.

Quinin, blue fluorescence.

Harmin and Harmalin, blue fluorescence.

Sanguinarin gives a red solution without fluorescence.

Shake out three times with petroleum ether, separate the solvent. Divide into two portions. One portion transfer to a distilling flask and distill off the solvent, noting the character of the residue, odor, taste, etc., as described below. This residue can then be tested as described in the text or used to furnish material to substantiate the results obtained when the following procedure is conducted.

The other portion is transferred to a separatory funnel. Shake out with three successive portions of 10 per cent sodium bicarbonate, collecting the alkaline liquid in a

clean separatory funnel. Reserve petroleum-ether solution. Add a slight excess of hydrochloric acid to the sodium bicarbonate solution and shake out with ether two or three times. Collect ether solutions in a clean separatory funnel, wash with water, discarding latter, filter ether into a small beaker and evaporate. The residue should contain the acid constituents of this fraction.

Then shake out petroleum ether solution with 5 per cent sodium carbonate, and treat the alkaline liquid exactly as described in the preceding paragraph. Then shake with 5 per cent sodium hydroxide and treat the alkaline liquid in the same way. Then wash the petroleum ether with water, discard latter, filter solvent solution and evaporate in a small beaker.

By this treatment four residues will be obtained. The acid constituents will be for the most part in the residue from the sodium bicarbonate shake-out; other acidic and resin-acid constituents in the residue from the sodium carbonate shake-out; phenolic bodies thymol, vanillin, and the like in the residue from the sodium hydroxide shake-out. The residue from the evaporation of the petroleum ether will contain the alkaloidal constituents, acetanilid, sulphonal and its allies, certain bitter and pungent principles, camphor, menthol, ascaridole and other substances of an alcoholic nature or which are unacted upon by alkalies.

Benzoic Acid, 120-121°
Cinnamic Acid, 135°
Ferulic Acid
Picric acid (very slightly)
Salicylic Acid, 156-157°
Epicarin (partly), 195–199°
Piperin, 128–129°
Narcyl (slightly)
Subcutin (somewhat), 195–196°
Chloretone, 80–81°
Brometone, 167°
Chloral Hydrated, 58°

Dormiol
Sulphonal, 125–126°
Tetronal, 85°
Neuronal, 66–67°
Veronal (slightly), 187–191°
Acetanilid, 113°
Acetphenetidin (Phenacetin, slightly), 134–135°
Antipyrin (trace), 112–113°
Cresol
Menthol, 43°
Thymol, 50–51°
Vanillin, 80–81°
Coumarin, 67°
Thujone boils 200°

Camphor, 175°
Santalol boils 300–310°
Eucalyptol boils 176°
Styrone (Cinnamic alcohol) boils 250°

Absinthiin, 120–125°
Cubebin, 132°
Hop Bitter (trace)
Ascaridole
Capsaicin
Zinzerone
Cannabis principle
Copaiba
Terebene boils 160–180°

Note the odor of the fractions; camphor, menthol, eucalyptol, copaiba, styrone, thujone, thymol, terebene, santalol, coumarin, and vanillin have characteristic odors. Most of these substances are usually found in liniments and mouth washes and in certain types of ointments, and a detailed procedure for their separation and identification in mixtures is given under "Liniments." It should be noted also that most of them are but slightly soluble in water and they will appear in largest amount in the residue from the alcoholic extract, which is insoluble in water.

Chloretone and neuronal have camphoraceous odors. Cubeb and ginger yield characteristic odorous principles in this fraction.

Remove a small quantity on the end of a glass rod or on a the end of a finger, and touch the tongue.

A pungent sensation indicates capsaicin, piperin, zinzerone.

Bitter taste indicates hop bitter, absinthiin, and cubebin.

Peppery sensation indicates chloretone, brometone.
Numbness indicates subcutin.

Tests on Residues Obtained by Shaking with Alkalies

Cover the dish containing the residue with a watch-glass and place on a covered water-bath. Note any sublimate that collects on the watch-glass, indicating vanillin, benzoic or salicylic acids. Salicylic acid sublimes more slowly than benzoic, and collects in quantity on the sides of the flask; benzoic collects in long stalactites having a brilliant luster. Cinnamic acid does not sublime. Treat a portion of the sublimate with water, pour into an evaporating dish and add a drop of ferric chloride solution; a purple color indicates the presence of salicylic acid.

Treat a portion of the residue with warm water, cool, filter, and treat with a few drops of ferric chloride, and in the presence of epicarin an intense blue color develops. Vanillin will give a blue color, but its presence is always affirmed by its characteristic odor, and it reduces ammoniacal silver oxide solution. Cresols give a transient blue color, the solution clouding almost immediately, and color passes rapidly to grayish green and muddy brown with finally the formation of a brown precipitate. Epicarin, warmed with concentrated sulphuric acid, yields a red-brown solution with a vivid green fluorescence.

Treat a portion of the residue with 2 to 3 c.c. of cold 10 per cent. potassium permanganate solution and warm slightly; if the odor of benzaldehyde develops, cinnamic acid is indicated.

If benzoic acid is indicated, dissolve a portion of the residue in dilute ammonia, evaporate and dissolve in water. Add ferric chloride, which will give a buff-colored precipitate in presence of benzoic acid. Ferulic acid gives the same kind of a precipitate with ferric chloride, and in addition it reduces Fehling's solution, differing thereby from benzoic.

Benzoic acid may be separated from salicylic by dissolving both in dilute hydrochloric acid, adding excess of bromin water, which precipitates the latter, filtering, boiling off the excess of bromin, and shaking out the benzoic acid with ether.

Tests on Residue from Evaporation of Petroleum Ether after the Alkaline Shake-out

Treat a portion of the material with 5 c.c. chloroform and 2 c.c. of concentrated potassium hydroxide, heat carefully, note odor, the presence of acetanilid being indicated by the evolution of phenol isocyanide.

Treat a portion of residue with dilute hydrochloric acid and water, placing a few drops on a water-glass, and add Mayer's reagent; if a precipitate is obtained, antipyrin is indicated. Boil another portion of this solution and then add a few drops of potassium bromide-bromate reagent; if a blue color appears, acetphenetidin is indicated. Treat a portion of residue with concentrated sulphuric acid; an orange-red color indicates piperin. This test cannot be depended upon unless the residue is white. Piperin should be crystallized out in petroleum ether, and its melting-point determined—128–129°.

Treat a portion of the residue with ammonium vana-

date; a green color, changing to blue, quickly disappearing, indicates subcutin. Treat another portion with formaldehyde-sulphuric acid, which gives, with subcutin, a salmon color changing to brown.

Dissolve a portion in water and treat the solution with ammoniacal silver nitrate, and warm. A reduction indicates chloral or dormiol.

It is necessary to distinguish between chloral and its amido compounds and other amido bodies such as acetanilid. A small amount of the residue should be warmed with potassium hydroxide and if there is no carbylamine odor it is almost certain that no amido substances are present. If the odor is obtained it may indicate acetanilid. The residue should then be heated in a small Erlenmeyer on the steam-bath with dilute sulphuric acid for an hour, not allowing the concentration to become great enough to produce charring, then diluted and shaken out several times with ether, which will remove the chloral. On evaporating the ether the chloral will be left. Chloral gives the reaction already mentioned, and in addition gives chloroform when warmed with dilute alkali. With alcoholic alkali it gives a formate and a chloride. When boiled with magnesium oxide and water it yields chloroform and magnesium formate. Bromal hydrated may be distinguished from chloral hydrate, since it will give bromoform on warming with dilute alkalies. Bromoform gives the carbylamine reaction, but when boiled with alcoholic potash it does not give a formate.

Trichloracetic acid gives the carbylamine reaction, but hot alkalies decompose it into chloroform and a carbonate.

Chloretone fragments, when thrown on the surface of water, rotate about as camphor does. An aqueous solution reduces ammoniacal silver nitrate in the cold and Fehling's solution on boiling. Alkalies decompose it on boiling, acetone being one of the products, recognized by the iodoform and the nitroprusside reaction. With concentrated potassium hydroxide, even in the cold, chloroform is one of the products of decomposition, hence on warming the residue with this reagent in the presence of an amido compound, carbylamine is formed. The formation of acetone distinguishes the product from chloral.

A solution of pyrogallol in pure 66 per cent H_2SO_4 gives a blue color when gently warmed with chloral, a ruby color with butylchloral, and a more or less violet to blue color with mixtures. On adding a large amount of water, the blue color changes to yellowish, and the ruby to violet.

Sulphonal, trional and tetronal are condensation products of ethylmercaptan and a ketone. They are usually found by themselves. They do not give any well-defined color or precipitation tests. Portions of the residue should be tested first by ignition with charcoal and then with anhydrous sodium acetate. If the charcoal reaction develops an odor of mercaptan and if hydrogen sulphide is evolved on heating with sodium acetate, these substances are indicated. The residue should then be recrystallized out of the solvent and the melting-point determined.

Neuronal when heated with dilute sodium hydroxide is decomposed, sodium bromide and cyanide being formed and diethylketone set free.

Coumarin, which resembles vanillin in the character of its odor, is separated from the latter by shaking out the vanillin by alkali when both are dissolved in a volatile solvent. It gives no color with ferric chloride. On boiling for half an hour with alcoholic alkali it yields coumaric acid. A solution of coumarin in strong alkali has a greenish-yellow color.

Ascaridole is an organic peroxide and will remain behind in the solvent after other substances are removed by shaking out with alkalies. If the solvent is allowed to evaporate at a low temperature over saturated ferrous sulphate and the mixture then shaken at a temperature above 30° C., basic ferrous sulphate will be precipitated and a combustible gas evolved.

If the residue is greenish or olive colored, dissolve a portion in absolute alcohol which has been saturated with hydrogen chloride. If a bright cherry red color develops, disappearing on dilution with water or more alcohol, Cannabis is indicated. The presence of active Cannabis principles is best determined by a physiological test on a dog. An alcoholic extract of the sample is diluted and shaken out with petroleum ether two or three times and the solvent cautiously evaporated. The residue is dissolved in a minimum quantity of alcohol, transferred to a gelatin capsule and placed well back on the dog's tongue, closing the mouth quickly and inducing swallowing by slapping the throat. Typical Cannabis manifestations are first vomiting and excitability, then incoordination, the animal losing control of its legs and the muscles supporting its head; finally exhaustion and deep sleep ensue.

To identify capsaicin in presence of ginger resin and

zinzerone, dissolve the residue in alcoholic potash, heat for half an hour in a boiling water-bath under a reflux, evaporate to dryness, take up with water and shake out with petroleum ether. Separate the solvent and wash with water until the washings are neutral. Then allow the solvent to evaporate spontaneously in a dish. The tip of the tongue is then applied to the residue or to the center of the bottom of the dish where the residue would naturally concentrate, when the presence of capsaicin will be apparent by its characteristic burning sensation.

Whenever possible the crystalline substances should be recrystallized out of water or dilute alcohol, filtered, washed, dried on porous tiles, and their melting-points determined.

Shake out three times with ether, separate the solvent, wash it with water. The following substances may be in this fraction.

ACIDS

Aconitic, 186°
Angelic
Atropic, 106–107°
Camphoric, 187°
Catechutannic
Cholalic
Creosotic, ortho, 163°, meta, 174°, para, 151°
Diiodosalicylic, 220–230°
Gallic, 220–240°
Ichthyol acids
Lauric, 43°
Lactic
Meconic
Monobrombenzoic, para, 251°
Monoiodosalicylic, 198°
Nitrobenzoic, ortho, 147°, para, 238°, meta, 148°
Oenanthic, 10–11°
Oxybenzoic, meta, 200°, para, 210°
Protocatechuic, 199–200°
Succinic, 182°
Tannic slightly
Trichloracetic, 52.5°
Tropic, 117–118°
Valeric
Veratric, 182°

Alkaloids

Caffein, slightly, 236°
Colchicin
Narcotin, slightly, 171°
Narcyl, slightly
Papaverin, slightly
Theobromin, 329–330°

Plant Principles other than Alkaloids

Aloe-emodin, 216–218° (228°)
Arnica principle
Chiratin
Chrysophanic acid, 191°
Citrullol (characteristic of colocynth and euonymus)
Colchicein, 149–151° (decomposition product of colchicin)
Columbin
Convallamarin, slightly
Cotoin, 130–131°
Elaterin (characteristic of elaterium and colocynth) soluble in alkalies
Emodin, 252°
Emodin monomethyl ether, 195°
Eriodictyol, 267° } phenolic ketones from eriodictyon (Yerba santa)
Homoeriodictyol, 223° } phenolic ketones from eriodictyon (Yerba santa)
Ergoxanthein
Filmaron, soluble in alkalies from ether solution
Gentiopicrin, slightly
Ginger resins
Helenin
Helleborin
Hop principle (bitter and amorphous)
Kaempferol, 274°
Lactucerin
Meconin, 102°
Paracotoin, 149–152°
Picrotoxin, 192–200°
Podophyllotoxin
Rhein, 318°
Saliretin (Hydrolytic product of salicin with acids)
Saligenin (Hydrolytic product of salicin with emulsin)
Santonin, 170–171°, partly
Sapogenins
Scopoletin, 204°
Scutellarin

Phenols and Phenol Derivatives

Alphanaphthol, 94°
Betanaphthol, 122°
Carbolic acid, 40°
Creosote
Creosote phosphite (Phosphotal)
Creosote valerate (Eosote)
Diosphenol, 82°
Fluorescein
Hydroquinone, 169° (Hydrolytic product of arbutin)
Methyl eugenol
Phenolphthalein, 250
Phloroglucinol, 200–209°
Picric acid, 122–125°
Pratol, Pratensol } (Characteristic of Trifolium pratense)
Pyrocatechin or catechol, 104°
Pyrogallol, 132°
Resorcinol, 109–110°
Vanillin, 80–81°

MISCELLANEOUS SYNTHETIC DRUGS

Acetanilid, 113°
Acetphenetidin, 134–135°
Anesthesin, 89–91°
Antipyrin, 112–113°
Aspirin, 135°
Bromacetanilid, para (Asepsin), 164°
Bromal Hydrate, 53°
Bromural
Butyl Chloral Hydrate, 78°
Chloral Formamide, 114–115°
Chloral Hydrate, 58°
Chloralimide, 153°
Chloralose, 185°
Chloral Urethane, 103°
Coryfin
Coumarin, 67°
Dormiol (Amylenechloral)
Epicarin, 195–199°
Ethyl acetanilid, 50°
Ethylideneurethane, 125–126°
Euphorin (Phenylurethane), 49–50°
Formanilid, 46°
Gallanol (Gallic acid anilid), 205°
Gallicin (Gallic acid methyl ester), 202°
Hedonal, 76°
Heliotropin, 37°
Hypnone, 140°
Methaform
Neuronal, 66–67°
Orthoform, trace, 141–143°
Propaesin, 74–76°
Propanol
Proponal, 145°
Pyramidon, 106–107°
Saccharin, 220°
Saligenin (Diathesin), 86°
Salophen, 187–188°
Subcutin, 195–196°
Sucrol (Dulcin), 173–174°
Sulphonal, 125–126°
Tetronal, 85°
Thymacetin, 136°
Trional, 76°
Trioxymethylene, 171°
Urethane, 48–50°
Valyl (Valerianic acid diethylamide)
Veronal, 187–191°
Cantharidin, 218°
Cholesterin, 145–148°
Lecithin

Note the color of the ether. If yellow, draw off 2 c.c. into a test-tube, add 1 c.c. ammonia, and shake. If the ammonia turns pink or crimson, emodin or other anthraquinone derivatives, or phenolphthalein are indicated. A blood-red color indicates ergoxanthein. A pinkish-yellow color, gradually deepening with a more pronounced pink shade, will be observed if aloes are present, this conclusion being further strengthened by a pronounced odor of aloes in the original material. A

blue fluorescence denotes the presence of scopoletin. A yellow color may indicate a great variety of substances, including Podophyllum and Trifolium.

Evaporate the entire ether solution over the steam-bath, using a fan as the last portion evaporates, to prevent overheating, and note the quantity of the residue. Note whether there are needle-like crystals present, characteristic of caffein and theobromine. Note the odor, which will indicate the presence of ginger resins, phenol, guaiacol, ichthyol, and coumarin.

Certain substances which are present in the petroleum ether fraction will appear now, being incompletely removed by that solvent. Thus, if salicylic acid, antipyrin, acetanilid, neuronal, veronal, trional, sulphonal, and acetphenetidin were found in the residue left on evaporating petroleum ether they will be found in this fraction.

Test a little of the residue cautiously by removing a small portion on the end of a rod or the finger. An intense sweet taste indicates saccharin. A numbness produced on rubbing the end of the tongue indicates propaesin, subcutin, and anesthesin. Pungency may indicate cotoin.

Treat a small amount of the residue with 2 c.c. dilute sulphuric acid, and warm; if the material does not completely dissolve, filter into another watch-glass. Add Mayer's reagent; a precipitate indicates antipyrin, colchicin, narcotin, the precipitate of colchicin being a deep yellow color.

Dissolve the residue in ether and divide into two portions. One portion can be reserved for tests described in the text or to substantiate the results obtained when the following procedure is conducted.

The other portion is transferred to a separatory funnel. Shake out with three successive portions of 10 per cent sodium bicarbonate, collecting the alkaline liquid in a clean separatory funnel. Reserve ether portion. Add a slight excess of hydrochloric acid to the sodium bicarbonate solution and shake out with ether two or three times. Collect ether solutions in a clean separatory funnel, wash with water, discarding the latter, filter ether into a small beaker and evaporate.

Then shake out the ether solution with 5 per cent sodium carbonate and treat the alkaline liquid exactly as described in preceding paragraph. Then shake with 5 per cent sodium hydroxide and treat the alkaline liquid in the same way. Then wash the residual ether solution with water, discard latter, filter solvent solution and evaporate in a small beaker.

By this treatment four residues will be obtained. The acid constituents will be in the residues from the sodium bicarbonate and sodium carbonate shake-outs; the phenolic constituents will be in the residue from the sodium hydroxide shake-out. Then the residue from the evaporation of the ether may contain alkaloids, most of the substances listed under Miscellaneous Synthetic Drugs, glucosides, and other plant principles not acids or phenols.

The residues should then be subjected to tests with the reagents described below. Dissolve in ether.

Remove 5 to 10 drops, and evaporate in a porcelain evaporating dish. Add 1 to 2 drops of concentrated sulphuric acid, and note the color.

Emodin, pink.

Elaterin, pink quickly changing to reddish yellow.

Picrotoxin, yellow, orange, red on warming, and gradually a reddish-brown, while the solution becomes fluorescent, observable on pouring the solution into a small test-tube.

Columbin, orange to red, throwing out brown flocks on dilution with water.

Helleborin, intense red gradually disappearing and a white precipitate separates.

Colocynth, bitter, yellow-brown.

Kaempferol, bluish fluorescence.

Cotoin crystals turn orange, while solution becomes bright yellow.

Paracotoin, yellowish brown.

Meconin, pale yellow gradually becoming pale violet.

Convallamarin, brown, becoming deep purple on standing.

An aqueous solution of convallarin gives a precipitate with tannic acid.

Santonin, yellow, with violet around isolated crystals; on diluting with water and adding $FeCl_3$ a violet color results.

Gentiopicrin, colorless, carmine on warming.

Gelsemic acid, yellow.

Narcotin, pale yellow, pink on edges, gradually red develops all through.

Papaverin, pale violet, soon fading.

Saligenin, bluish-red.

Many other substances give a brownish or a greenish-brown color, which is not characteristic.

Next remove 5 to 10 drops, evaporate in a porcelain dish, and add 1 to 2 drops of Froehde's reagent.

Colocynth bitter gives a dirty red, cherry-red.

Elaterin, pink, yellowish green, deep green.

Aloe-Emodin, pink to red-pink.

Meconin, pale yellow, pale green.

Narcotin, deep green.

None of the other plant principles give characteristic colors.

Next remove 5 to 10 drops, evaporate in a porcelain dish, and add 1 to 2 drops of ammonium vanadate reagent.

Meconic acid, purple, deep blue; gradually fades, very characteristic.

Colocynth bitter, red, blue in thin layers, pink, gradually deep crimson.

Elaterin, intense blue, soon fading to dirty yellow; undissolved crystals, orange, finally deep green, very characteristic.

Emodin, bright red, liquid soon turns brown.

Phenolpthalein, deep orange, pink on edges.

Meconin, crystals pale yellow at moment of solution; solution turns pale green, yellow, gradually pale red.

Subcutin, green to blue, disappearing quickly.

Santonin, no color.

Narcotin, brick red, pink in thin layers.

Papaverin, purple, blue, green, gradually deep blue.

Propaesin, purple, gradually fading to brown and gray.

Remove 5 to 10 drops, evaporate in a porcelain dish, treat residue with 2 c.c. water, warm, then cool, and add 2 to 5 drops ferric-chloride test solution.

Green or greenish-black color indicates tannic or gallic acid.

Meconic acid, deep red.

Cotoin, violet-brown.

Aspirin, usually shows a violet color, deepening on standing.

Phenol blue.

Epicarin, blue.

Saligenin, indigo blue.

Salicylic acid, violet.

Pyrogallol, orange-yellow.

Guaiacol, orange-red, slowly fading and solution becoming turbid.

Hydroquinone, yellow-orange, green-black precipitate. This precipitate may be crystallized pure out of boiling water. It is soluble in alcohol to a yellow solution, and gives a green solution with ammonia, turning brown on exposure to air. A solution of hydroquinone reduces Fehling's solution.

Phloroglucinol, blue-violet, violet fading rapidly.

Resorcinol, blue-violet.

Vanillin, blue.

Coumarin, no color.

Catechol, green, changing to violet or red on the addition of sodium bicarbonate, and restored to green on the cautious addition of sodium hydroxide.

Alpha naphthol, white or purplish white precipitate, or a reddish color turning violet.

Beta naphthol, opalescent solution sometimes with a green tint.

Diosphenol, the characteristic component of buchu oil, is soluble in alcohol and in this solution gives a dark green color with ferric chloride.

Remove 5 to 10 drops, evaporate in porcelain dish, add 1 to 2 drops concentrated nitric acid, and note reaction. Then evaporate and add alcoholic alkali.

Cotoin with nitric acid, deep blue, black, considerable action, brown-orange; very characteristic.

Paracotoin, yellowish brown.

Ergoxanthein, deep orange.

Santonin, no characteristic reaction with nitric acid on evaporation and addition of alkali, orange.

Elaterin chars on adding nitric acid.

Subcutin on adding alkali gives blood-red color and a fragrant odor.

Colchicin, blue.

Gelsemic acid, yellow, orange; add ammonia, which produces a blood-red color, very permanent.

Phenols

In order to test for phenols it is necessary to remove acids and tannins. The residue should be dissolved in water, lead acetate added drop by drop until no further precipitation occurs and the solution filtered. The filtrate is then shaken out with ether, the ether solution filtered, evaporated, and the residue tested with ferric chloride. Catechol is precipitated by lead acetate.

Certain acids are best removed by dissolving the residue in ether and shaking out with sodium carbonate solution two or three times. Subsequent shaking with sodium or potassium hydroxide will remove the phenols, and on separating the alkaline solution, acidifying, extracting with ether, separating and evaporating the ether solution, the phenols may be recovered. Pyrogallol, catechol, and hydroquinone will be lost by this treatment, owing to oxidation in alkaline solution.

If phenolic compounds are indicated (color reaction

with $FeCl_3$) evaporate 5 c.c. of the ether solution in a test-tube, cool residue, add an equal bulk of phthalic anhydride, moisten with a drop or two of sulphuric acid, place in an oil or sulphuric acid bath heated to 160°, and maintain at this temperature three minutes. Cool, add 2 c.c. water and 1 to 2 c.c. sodium hydroxide until alkaline, filter, and observe color.

Carbolic Acid gives phenolphthalein, the solution being deep pink or beet red, not fluorescent.

Guaiacol gives a solution having a deep violet to permanganate shade, not fluorescent.

Hydroquinone gives a deep purplish-red solution with a blue fluorescence.

Resorcinol gives fluorescein, solution being yellowish brown with green fluorescence.

Catechol gives blue solution.

Pyrogallol gives a deep olive-green solution, appearing black in bulk. Reports say rose red.

Alpha naphthol gives a dark bluish-green solution, appearing black in bulk.

Beta naphthol gives pale yellowish-green solution with a deep blue-green fluorescence.

Phloroglucinol gives a mahogany-brown solution.

Vanillin gives a pale olive-green solution.

Thymol may yield a yellowish-brown solution. Reports say blue.

When a phenol is dissolved in concentrated sulphuric acid and treated with a nitrite, colored solutions result, which, after diluting and adding excess of alkali are brown, blue, or green.

Catechol reduces Fehling's solution and silver nitrate in the cold. Lime water causes a reddish or brown color.

Pine wood moistened with hydrochloric acid is colored blue by an aqueous solution of catechol.

Phloroglucinol reduces Fehling's solution and stains pine wood moistened with acid a violet red color.

When a naphthol is warmed with chloral hydrate, the alpha compound gives a ruby-red color and the beta a blue. If hydrochloric acid is present the colors are dark greenish blue and yellow respectively. If zinc and hydrochloric acid are the reacting agents on the chloral solution, alpha naphthol yields a dark violet-blue color, and the addition of water throws out a violet flocculent precipitate, which is soluble in alcohol to a fluorescent violet liquid. Under the same conditions the beta compound gives a dark-brown color, water throwing out a greasy precipitate which is soluble in alcohol to a yellow liquid having a blue fluorescence.

If saccharin is indicated by the sweet taste, and the residue gives a blue color with ferric chloride indicating salicylic acid or phenols, treat a portion with dilute hydrochloric acid, warm, filter, cool, and add bromin water, allow the precipitate to settle, then filter and wash. Boil filtrate until bromin is expelled, add a small piece of sodium hydroxide, evaporate the solution, fuse in an oil-bath to 250° C., cool, add water, and transfer to separator, add hydrochloric acid and shake out with ether, evaporate ether, test residue with ferric chloride, when a violet color, due to formation of salicylic acid from saccharin, will be observed.

Dulcin may be differentiated from saccharin by dissolving in ether and shaking with alkali, which removes the saccharin; the ether is then washed, filtered, and evaporated, leaving the dulcin.

Test for cantharidin by dissolving a portion in alcohol and applying the solution to the arm, which will blister if this substance is present.

Santonin gives a red color with warm alcoholic alkali.

Anesthesin, subcutin, propaesin, derivatives of amido-benzoic acid, all appear at this point.

Subcutin gives salmon gradually to brown with formal-dehyde-sulphuric acid reagent, and green to blue color with ammonium vanadate.

Propaesin gives, with ammonium vanadate, a purple gradually fading to brown and gray.

Propaesin may be hydrolyzed by boiling with NaOH under a reflux; propyl alcohol is one of the products, and will be apparent because of its odor; from the alkaline solution mineral acids will precipitate the acid radicle.

Anesthesin on hydrolysis gives ethyl alcohol and paramido benzoic acid. If the alkaline solution is treated with iodin the iodoform reaction is obtained. When a small quantity of anesthesin is treated with 100 c.c. of water and a little hydrochloric acid followed by a few drops of sodium nitrite and an equal quantity of beta naphthol, an intense cherry red color results.

Aspirin differs from salicylic acid in giving no precipitate with bromin water. Pure aspirin which has not been exposed to the action of water gives no color with ferric chloride. But it gradually hydrolyzes when treated with water, and if ferric chloride is present a violet color soon appears, deepening on standing.

Paracotoin when boiled with caustic alkali yields a substance having an odor similar to coumarin.

Pratol and pratensol, from red clover, come out in

this fraction. The latter is much more soluble in ether. They are soluble in alkali carbonates and hydroxides, the solution being yellow. Pratol gives no color with ferric chloride. Partensol in alcoholic solution, gives a greenish-black color.

Test a portion of the dry residue by heating with charcoal and another with anhydrous sodium acetate. If mercaptan is given off in former and hydrogen sulphide in latter, sulphonal, trional, and tetronal are indicated.

Veronal sublimes on heating. On boiling with sodium carbonate it is decomposed with liberation of ammonia. If 1 to 2 c.c. of a saturated aqueous solution are treated with two drops of Millon's reagent, a gelatinous white precipitate is obtained. When added to potassium hydroxide fused in a nickel crucible, and heated for two minutes, the cold mass, on dissolving in water, should give the Prussian-blue test with ferrous sulphate; on adding excess of acid, and shaking out with ether, an oily mass is extracted having the odor of rancid butter, soluble in water, the solution giving a wine-red color with ferric chloride.

Anthraquinone Derivatives

Several important vegetable drugs, Aloes, Rhubarb, Senna, Cascara, the Buckthorns and Chrysarobin contain one or more derivatives of anthraquinone; chrysophanic acid, emodin, aloe emodin, emodin monomethyl ether and rhein, and these derivatives will appear in this fraction. The separation and identification of the anthraquinone derivatives is possible only when one has

a considerable quantity of material to work with, much more than is usually offered as a sample of a medicine, and for practical purposes about all that is necessary to do is to identify the substance as a derivative of anthraquinone. They are all closely related to alizarine which is a dihydroxyanthraquinone. Rhein is a true acid and contains a carboxyl group, the others do not. The reports thus far available indicate that these substances are distributed among the drugs above mentioned in the following way:

Aloes	Rhubarb	Senna	Cascara
Aloe emodin	Chrysophanic acid	Rhein	Emodin
	Emodin	Aloe emodin	
	Aloe emodin		
	Emodin monomethyl ether		
	Rhein		

Buckthorn	Chrysarobin
Emodin	Chrysophanic acid
Chrysophanic acid	Emodin monomethyl ether
Rhein	

If aloes or rhubarb are present in a preparation the characteristic odor of the drug will have been apparent when the alcohol extract was being concentrated. The ether fraction if it contains these derivatives will be yellow and will leave a yellow residue on evaporation. The ether solution when shaken with alkali will give a magenta color with the anthraquinone derivatives of Rhubarb, those of Senna and the Buckthorns also give intense crimson or magenta shades, with Cascara the color is lighter and more pinkish and with Aloes the color develops gradually, the yellow color of the ether solution disappearing when shaken with the alkalies.

Chrysophanic acid gives a deep purple-red color with caustic alkalies and if the alkaline solution is heated with zinc dust, the color is discharged, leaving a yellow liquid, on adding water and a few drops of hydrogen peroxide, the color is restored. An alkaline solution of phenolphthalein is reduced by zinc and the color is not restored by hydrogen peroxide.

Emodin can be separated from chrysophanic acid by shaking an ether solution of the substances with dilute sodium carbonate which will remove the former.

Emodin dyes wool yellow; the color is stripped by ammonia, and gives a second dyeing. An alcoholic solution of emodin on evaporation with ferric chloride leaves a yellow residue; phenolphthalein under similar conditions leaves a pinkish residue, with odor of phenol, the color disappearing on cooling or in the presence of moisture. Phenolphthalein goes on to wool, but there is no color imparted.

Phenolphthalein will seldom be found in a preparation containing the anthraquinone drugs, but if suspected, the residue should be dissolved in dilute sodium hydroxide and treated with an excess of iodin solution, followed by hydrochloric acid, which precipitates tetraiodophenolphthalein. After cooling for an hour below 15° C. the solution is filtered, the excess of iodin removed by sodium sulphite, and the solution extracted with ether or benzol to remove the anthraquinone derivatives.

Tetraiodophenolphthalein, also called nosophen, is insoluble in water and acids, but dissolves in ether, chloroform, and alkalies. It melts with decomposition at about 225° C.

Kaempferol is a yellow flavone derivative occurring

in Senna and will appear in this fraction. It may be separated from the anthraquinone derivatives by dissolving the residue in ether and shaking out with dilute sodium carbonate, which removes the kaempferol before the aloe emodin. On acidifying the alkaline solution, extracting with ether, shaking again with dilute sodium carbonate the kaempferol can finally be obtained pure. It gives a yellow color with alkalies and a blue fluorescent solution in strong sulphuric acid.

Eriodictyol and homoeriodictyol give yellow solutions with alkalies, darkening rapidly on exposure to the air. They may be removed from ether by sodium carbonate, and a sodium derivative of the latter will separate out, and on washing with water and dissolving in acetic acid, the compound is broken up and may be shaken again by ether. The sodium carbonate solution of eriodictyol darkens on exposure. The aqueous or alcoholic solution of eriodictyol gives greenish brown to pure brown with ferric chloride. The alcoholic solution of homoeriodictyol gives an intense red brown. The aqueous solution of homoeriodictyol is not precipitated by lead salts, but eriodictyol is thrown out by basic lead acetate.

Antipyretics

Both acetanilid and acetphenetidin will have been indicated in the petroleum ether fraction. If antipyrin has been indicated in this fraction, by the precipitate produced by Mayer's reagent, dissolve a portion in a little water and add to a solution of sodium nitrite slightly acid with sulphuric acid. A green color and sometimes a green precipitate is produced if antipyrin is present.

The color changes to purplish red on heating. Pyramidon gives a blue to violet color.

Pyramidon is the only substance in common use which might be mistaken for antipyrin. It melts at 108°, gives a bluish-violet color with ferric chloride, and reduces silver nitrate after first giving a blue color, antipyrin undergoing no change with silver nitrate.

All of these antipyretics may be completely removed from an acid solution by sufficient shaking with chloroform, and in common practice will appear in largest amounts in the next fraction discussed.

To separate the antipyretics, antipyrin, acetanilid, and acetphenetidin from each other and from caffein, dissolve the residue in chloroform and shake out with dilute sodium hydroxide to remove acids and phenols. Transfer chloroform to a small flask, evaporate, treat residue with about 10 c.c. of dilute sulphuric acid (1 in 10) and digest on the steam-bath. The flask may be fitted with a two-hole stopper containing an outlet and inlet tube, the latter reaching nearly to the surface of the liquid, and the former just inside the cork, with its exterior end immersed in water containing barium carbonate. A gentle stream of air is blown through the inlet tube in order to carry off the vapors of acetic or formic acid produced by hydrolysis of the anilides or phenetidins. The flask should be rotated from time to time to wash down any crystals which may have adhered to the sides. When the contents are reduced about one-half, a further quantity of acid is added and digestion continued until the volume is again reduced.

Dilute the liquid with water and shake out with chloroform three or four times to remove antipyrin and caffein,

leaving in solution the anilin and phenetidin sulphates. Separate and evaporate the chloroform, dissolve the residue in water, add picric acid solution drop by drop until no further precipitation of antipyrin picrate takes place, filter, shake out with chloroform, wash chloroform with dilute alkali to remove the picric acid and then evaporate the chloroform, leaving a residue of caffein.

The solution containing the sulphates of anilin and phenetidin is warmed to drive off any adhering chloroform, cooled, and treated with iodin solution which will precipitate the phenetidin in the form of an iodin compound. Filter, add sulphurous acid to destroy excess of iodin, add excess of sodium hydroxide, and shake out with ether, which will remove anilin. On evaporating the ether the anilin will be left as a residue and can be identified by the carbylamin reaction.

The aqueous mixture containing the barium carbonate is filtered and tested for formic and acetic acids. Formanilid will yield formic acid on hydrolysis with acid.

If pyramidon is present it will follow the same course as antipyrin.

Bitter Drugs

If Podophyllum is present a yellow coloring matter from the drug comes out in this fraction. It gives a bright yellow color with ammonia. If the coloring matter is boiled with water, cooled, shaken out with ether and again treated with ammonia the color will be amber.

Citrullol occurring in Colocynth and Euonymus will

appear in this fraction, and is probably the cause of the color tests noted. Pure citrullol, when dissolved in chloroform, followed by acetic anhydride and concentrated sulphuric acid, will produce a series of color reactions similar to the phytosterols. Colocynth contains a small quantity of an alkaloid which will appear in the shake out from alkaline solution.

Gentian will yield a certain amount of bitter-tasting principles. Gentiopicrin on hydrolysis with dilute sulphuric acid in alcoholic solution yields gentiogenin, which is thrown out on dilution. This substance is soluble in 95 per cent alcohol and if allowed to overlay concentrated sulphuric acid, a blue zone will appear at the point of contact.

Chiratin is a yellowish, bitter substance occurring in chirata. It dissolves readily in hot water and gives a copious precipitate with tannic acid.

Hops if present will yield an amorphous bitter substance in this fraction.

Quassia bitter is removed to a slight extent only by ether, but will be found in the chloroform fraction.

Picrotoxin is bitter. It dissolves in alkalies, from which solution it cannot be removed by immiscible solvents. When evaporated with nitric acid it leaves a reddish-yellow residue which turns red when moistened with aqueous alkali. A solution in concentrated sulphuric acid, treated with potassium nitrate, gives a red to violet color when strong alkali hydroxide is added. It will dissolve in hot water, the solution reducing Fehling's solution and ammoniacal silver oxide. It is not precipitated by lead salts or tannin. If a dilute aqueous solution is added to a bowl containing a few small fish, the

creatures will soon begin to swim with uncertainty, lose their balance and rise to the surface, lying on their sides and frequently opening their mouths and gill covers.

Ergoxanthein, an orange-yellow substance from ergot, will be found in this fraction. An ether solution shaken with cold saturated sodium bicarbonate colors the latter violet. If the ether solution is shaken with ammonia, the alkaline liquid separated and precipitated with basic lead acetate, the precipitate will color a cold saturated borax solution a red-violet color.

Meconic acid and meconin are characteristic opium principles. The substances can be separated by dissolving the residue in water and shaking out the meconin with chloroform. Meconic acid is then precipitated by lead acetate, the precipitate washed with water, decomposed by hydrogen sulphide in the presence of water, the solution filtered and shaken with ether, which on evaporation will leave pure meconic acid.

An aqueous solution of meconic acid gives a deep red color with ferric chloride, which is decolorized by stannous chloride and restored by potassium nitrite.

Scutellarin, when treated with water and sulphuric acid, is dissolved with the formation of scutellarein, $C_{15}H_{10}O_6$, and glucuronic acid; on pouring the solution into considerable water the former is precipitated. Scutellarein dyes wool reddish-brown with chrome mordant, brownish-yellow with aluminum, lemon with tin, and olive with iron. The hydrobromide, hydrochloride, and sulphate are intensely colored. Glucuronic acid in dilute alcohol gives a green color when treated with alphanaphthol and concentrated sulphuric acid, with more water the color changes through blue to violet,

and even red, the green color being regenerated by adding concentrated sulphuric acid.

Scutellarin gives an orange-yellow barium salt.

Now shake out the acid solution three times with chloroform, when the following substances, if present, will go into solution:

ALKALOIDS

Berberin traces
Caffein, 236°
Colchicin
Geissospermin, 160°
Hydrastin, partly, 132°
Narcein, partly, 145°
Narcotin, 171°
Narcyl base (Ethylnarcein)
Oxyacanthin, 210°
Papaverin, 147°
Piperin, 130°
Quebrachin, 214–216°
Theobromin, 329–330°

PLANT PRINCIPLES OTHER THAN ALKALOIDS

Columbin
Digitoxin, 240°
Elaterin (Characteristic of Elaterium and Colocynth)
Emodin with other Anthraquinone derivatives that may not have been completely removed by ether.
Gitalin
Helleborin
Picrotoxin, 192°
Polygalic acid, slightly
Quassin (Alpha- and Beta-picrasmin)
Santonin, 170–171°
Santoninic acid
Scopoletin, 204°
Senegin, slightly
Strophanthidin
Strophanthin, slightly

MISCELLANEOUS SYNTHETIC DRUGS

Acetphenetidin, 134–135°
Antipyrin, 112–113°
Betanaphthol benzoate, 110°
Hippol (Methylene hippuric acid), 151°
Methylene Blue, very slightly

Evaporate the chloroform solution cautiously over the steam-bath, using fan, and note the appearance of the residue.

Methylene blue gives a blue color.

Berberin and colchicin give a yellow residue (the latter will have been indicated in the ether fraction).

Caffein and theobromin give needle-like crystals.

Taste residue and note whether it is bitter, indicating quassin.

Dissolve the residue in a small amount of chloroform, evaporate 5 to 10 drops on a watch-glass, dissolve residue in 1 to 2 c.c. dilute sulphuric acid, and add Mayer's reagent; a precipitate indicates the presence of some alkaloid, but not caffein or theobromin, and if on standing there is a gradual liberation of iodin the presence of oxyacanthin is indicated. If no precipitate occurs, add 1 c.c. solution of iodin and potassium iodide; a precipitate indicates caffein, theobromin, narcein, and other substances. If caffein were present in the original material, it would have been found to some extent in the ether fraction, unless it was present in very small amounts only. Antipyrin would have been previously indicated; piperin would have been found before, as well as elaterin, emodin, picrotoxin, santonin, columbin, and other bitter principles.

Transfer the chloroform solution to a separatory funnel and shake out with 10 per cent sodium bicarbonate solution two or three times. Reserve the chloroform solution. Collect the alkaline solutions in a fresh separatory funnel, add an excess of hydrochloric acid and shake out with chloroform. Collect the solvent in another funnel, wash with water, filter into a beaker and evaporate. Then shake out the chloroform solution with 5 per cent sodium carbonate, treating the alkaline liquid as above, and then shake out with 5 per cent sodium hydroxide.

The alkaloids and certain other substances, columbin, digitoxin, gitalin, acetphenetidin, acetanilid, and santonin will have been left behind in the solvent after shaking out with the three alkaline reagents.

The substances removed by the alkalies and those remaining behind are then to be submitted to the color tests indicated below.

(If when examining the alkaloidal residue, the color reactions indicate mixtures, the residue may be purified by dissolving in dilute acid and adding Mayer's reagent drop by drop until precipitation is complete. Filter, wash with water, dissolve precipitate in alcohol, pass in hydrogen sulphide, filter off the sulphide of mercury, dilute with water, add ammonia, shake out with chloroform, separate, and evaporate the solvent. Caffein, theobromin, and piperin are not precipitated by Mayer's reagent and will remain in solution after the other alkaloids have been thrown out. Add excess of iodin in potassium iodide, rotate the container, filter off the iodin compound and decompose it with sulphurous acid. Filter if necessary, add ammonia, and shake with chloroform, which on evaporation will yield a residue of the pure substance.)

Evaporate 5 to 10 drops of the chloroform solution of the different fractions in porcelain evaporating-dishes, cool, add 1 to 2 drops concentrated sulphuric acid, and observe the color.

Narcein, deep brown at moment of solution, then yellow, gradually becoming green, and finally blue.

Narcotin, pale yellow, gradually pink on edges, and gradually a red color develops through the mixture.

Papaverin, pale violet, soon fading.

Colchicin, yellow. (If this alkaloid is suspected, add a drop of nitric acid, when the color will change to green, blue, violet, wine-red and finally green, addition of sodium hydroxide in slight excess then gives an orange red.)

Quebrachin, blue color gradually develops, brought out more intensely by addition of lead peroxide or bichromate (in the latter case the mixture soon turns brown).

Geissospermin, blue.

Columbin, orange changing to deep red.

Hydrastin gives a faint yellow, deep purple on heating.

If a trace of nitric acid is present, a yellow color is produced, and with a larger proportion the color is orange-red.

Digitalis glucosides, red, more intense on warming; expose to fumes of bromin and a violet color appears.

Digitoxin, green.

Elaterin, pink quickly changing to reddish yellow.

Emodin, pink.

Picrotoxin (see ether fraction).

Quassin, no characteristic color. (If no characteristic color develops add a few grains of sugar which will produce a red color if quassin is present.)

Strophanthin, green, greenish yellow, brownish green, finally dirty brown; warmed to 50° to 60°, the green color changes to dark olive, dark brown, violet, dark violet-blue, black with violet tint. Not a common substance, and not removed to any great extent by chloroform, most of it remaining in the aqueous solution after the treatment with immiscible solvents.

Santonin, yellow, violet around isolated crystals.

Saponin, yellow, violet shade gradually appears.

Polygalic acid, reddish yellow, gradually red, deep red, and, on warming, dark violet.

The color reactions given with sulphuric acid are usually only characteristic when the substances are pure and alone. Thus if resorcinol were present at the same time as narcein, and had not been entirely removed by ether, a crimson color would appear; or if a trace of tannin were present with hydrastin, narcotin, or narcein, a green color would be obtained. The reaction with resorcinol and sulphuric acid is very characteristic for narcein. However, if one follows the directions for separating the various principles occurring in this fraction the alkaloids should be free from these contaminating substances.

Evaporate 5 to 10 drops of the chloroform solution, and treat the residue with 1 to 2 drops Froehde's reagent.

Narcein, greenish brown.

Narcotin, deep green; characteristic.

Hydrastin, sage-green.

Papaverin, purple, gradually blue.

Oxyacanthin, violet changing to yellowish green on edges.

Saponin, dirty yellow, violet shade develops on edges, changing to indigo blue.

Colchicin, yellow.

Tests of the other substances which were also removed partially by ether, will not be repeated here.

Evaporate 5 to 10 drops of the chloroform solution and treat the residue with 1 to 2 drops of ammonium vanadate.

Narcotin, brick-red, pink in thin layers.

Narcein, reddish brown.

Papaverin, purple, blue, green, gradually deep blue; characteristic.

Colchicin, yellowish green.

Hydrastin, pink, bright red, gradually brick-red.

Saponin, violet, purplish brown; indigo-blue on edges.

Oxyacanthin, dirty violet to reddish violet.

Evaporate 5 to 10 drops of chloroform solution, and treat the residue with 1 to 2 drops formaldehyde-sulphuric acid.

Narcotin, purple to slaty, soon fading.

Narcein, deep brown, green on edges, gradually deepening.

Papaverin, purple, violet, crimson; characteristic.

Colchicin, crystals reddish, liquid yellow.

Hydrastin, no reaction.

Evaporate 5 to 10 drops of chloroform solution, and treat the residue with 1 to 2 drops nitric acid.

Narcotin, deep yellow.

Narcein, yellow, fading.

Papaverin, yellow.

Colchicin, deep purple; characteristic.

Hydrastin, yellow.

Geissospermin, purple-red, disappears on heating.

Polygalic acid, ruby-red; on adding more nitric acid the color becomes brighter, until finally bright yellow.

If caffein or theobromin are indicated, perform the murexide test. Dissolve the crystals in hydrochloric acid, add a crystal of potassium chlorate and evaporate over the steam-bath. Cool the residue, add a few drops of ammonia, and note the color produced, which should be a brilliant purplish pink. It is decolorized by caustic alkali.

Caffein and theobromin may be partially separated from each other by treating a residue with cold benzol in which theobromin is but slightly soluble. Theobromin forms a very characteristic compound with silver nitrate. Treat the crystals with 3 to 5 c.c. of water and about 6 c.c. of sodium hydroxide solution, followed by 1 c.c. ammonia and 1 c.c. silver nitrate 10 per cent. Shake the mixture and solidification will take place. On warming to 60° the mass will liquefy and on cooling a transparent jelly results.

Quassin.—Dissolve in chloroform, shake with bromin water in excess, separate chloroform and shake it with ammonia. The color due to bromin is immediately destroyed, and if quassin be absent both the chloroform and ammonia will be colorless; in presence of quassin the ammonia will be colored bright yellow. Substances from Calumba, Colocynth, Cocculus Indicus, and Chirata do not give any similar reaction. If picric acid is present, it may be removed by shaking the chloroform solution with sodium hydroxide before adding bromin water.

Hydrastin.—A solution of the residue in dilute acid gives a precipitate with potassium bichromate, which, on separating, gives a bright-red color when moistened with sulphuric acid.

A solution of hydrastin in dilute sulphuric acid should be treated with a drop of permanganate. The color of the reagent is immediately discharged, and an intense blue fluorescence develops. The picrate, recrystallized from boiling alcohol, melts 165–170° C.

Additional reactions for hydrastin, hydrastinin and narcotin. A solution of hydrastin 1 : 300 in alcohol, of

hydrastinin 1 : 100 in alcohol, and of narcotin 1 : 100 in dilute sulphuric acid and 0.1 c.c. added to 2 c.c. concentrated sulphuric acid will give the following color reactions: With 0.1 c.c. gallic acid 1 : 20 green to blue; with guaiacol or catechol 1 : 20, red tint changing to violet on warming; with morphin, violet. If hydrastin or narcotin be oxidized by acid solution of permanganate, opianic acid is produced, and on adding alcohol until a 1 per cent solution with 2 c.c. concentrated sulphuric acid, the following reactions will take place: With 0.1 c.c. gallic acid a blue color, fading to brown on warming; with guaiacol, red becoming intense blue on warming; with alpha naphthol, gooseberry-red; with beta naphthol, wine-red; with codein in alcohol 1 : 20, violet turning blue on warming.

Hydrastinin hydrochloride solution blackens instantly with Nessler's reagent. Morphin, apomorphin, and picrotoxin precipitate mercury from the reagent. The color reaction of hydrastinin with sulphuric acid, Froehde's reagent and ammonium vanadate are the same as those given by hydrastin. Its solution in dilute sulphuric acid when treated with a drop or two of permanganate shows fluorescence on dilution.

Oxyacanthin liberates iodin from iodic acid and from potassium iodide in dilute sulphuric acid, hence when performing the precipitation test with Mayer's reagent, the gradual appearance of liberated iodin will indicate oxyacanthin. It gives Prussian blue with ferric chloride and potassium ferricyanide. Canadin, an alkaloid accompanying hydrastin in Hydrastis root, gives the same reactions.

Gitalin is a glucoside from digitalis, and is the chief

component of commercial digitoxin. It is precipitated by tannin. The tannin compound may be filtered off, washed with water, decomposed by lead or zinc acetate and the gitalin recovered by shaking with chloroform. It is decomposed gradually by water, ether, and carbon disulphide. The aqueous solution froths on shaking. It gives a reducing sugar when boiled with water or alcohol. Sulphuric acid containing ferric chloride produces a violet color. When dissolved in acetic acid, ferric chloride added and then treated with sulphuric acid containing ferric chloride, the acid becomes indigo-blue, and the zone of contact violet.

Papaverin, narcotin and narcein are three opium bases which will appear in this fraction. The color tests noted are given by the separate individuals, and will be modified in a residue of the mixed alkaloids. The reactions with ammonium vanadate and formaldehyde sulphuric acid will be characteristic enough, even with a mixture, to indicate their identity. It has been claimed that pure papaverin gives no characteristic color tests and that the reactions attributed to it are caused by cryptopin. Narcein is not precipitated by Mayer's reagent hence the other two bases can be separated from it by precipitating an acidulated solution with the reagent, filtering and shaking out the acid solution with chloroform to recover the narcein. The precipitate of papaverin and narcotin is then treated with alcohol and subjected to the action of hydrogen sulphide, filtered, the alcohol evaporated, the liquid diluted with water, rendered slightly acid, and the alkaloids removed by chloroform. After evaporating the chloroform, the residue is dissolved in the least quantity of hydrochloric

acid, diluted with water to a $\frac{1}{4}$ per cent solution, from which the papaverin is precipitated by potassium ferricyanide, and after filtering and adding ammonia, the narcotin is shaken out with chloroform.

On mixing papaverin ferricyanide with formaldehyde-sulphuric acid, a light-blue color is produced, soon changing to violet and finally green, the color then fading to brownish yellow. If selenious acid and sulphuric acid is used the color is greenish blue which becomes deep blue. Papaverin solutions are not precipitated by Marme's reagent. The picrate melts 179–181°. Narcotin picrate melts 141°.

Narcein is precipitated from acid solution by iodin, and on removing the excess of iodin by cautious addition of ammonia, the precipitate is found to be blue. Weak iodin solutions color a narcein residue dark blue; on dissolving in boiling water a colorless solution results from which violet or blue crystals separate on cooling. The picrate melts 127–128°.

Colchicin dissolves easily in water. The aqueous solution does not give a precipitate with potassium iodide and the base can thereby be distinguished from berberin. If colchicin occurs with other substances which have not been separated by the alkaline shake-outs, the residue should be extracted with water, filtered, rendered slightly acid with hydrochloric acid and precipitated by iodin solution. The precipitate is filtered off, dissolved in sulphurous acid, neutralized and the colchicin recovered by means of chloroform. The residue will then show the characteristic color reactions already described. An aqueous solution of colchicin heated on the steam-bath for one-half hour with 5 drops

of 20 per cent hydrochloric acid and subsequently treated with 3 to 5 drops of ferric chloride solution will develop a green color, and on cooling and shaking out with chloroform the latter will separate either yellowish or permanganate red, depending on the amount of colchicin present. If the colored liquids are too opaque, the mixture must be diluted with water.

Add sufficient ammonia water to render the acid solution distinctly alkaline, and note the appearance. A green color indicates apomorphin. If the acid solution was red, due to the presence of sanguinarin, the red color will disappear on the addition of ammonia. If a red color appears on the addition of ammonia, physostigmin is indicated. The following drugs will cause a fluorescence: manaca, sumbul, Hydrangea, Hydrastis, Gelsemium, and pichi, which gives a blue fluorescence with ammonia. Now shake out three times with petroleum ether. Wash the combined solvents with water, filter into a beaker, and evaporate over the steam-bath, using fan. The following substances will be removed:

Acoin base, trace
Aconitin, trace, 182–186°, slow heating
Alypin
Anilin
Atropin, trace, 112–113°
Benzoylecgonin 90° when hyd., 195° anhyd.
Betaeucain base
Brucin, trace, 178°
Cephaelin, partly
Capsicin
Chelerythrin
Cocain, 98°
Conhydrin, 118–121°
Coniin
Emetin, trace
Gelsemium bases, small amount
Gujasanol base
Holocain base, trace
Hydrastinin, 116–117°
Lobelin
Lupanin
Lycoctonin
Methylconiin
Nicotin
Novocain base, 51–60°
Peronin base, somewhat

Physostigmin, trace
Quinin, traces, 171–172°
Quinolin
Rubijervin, trace
Sanguinarin, trace
Spartein
Stovain base
Strychnin, partly, 265–269°
Taraxacum base (Cholin)
Tropacocain, 49°
Trimethylamin
Veratrin, trace
Yohimbin, trace
Pyramidon, 106–107°

Note the appearance of the residue after the solvent is evaporated.

Liquid: nicotin, spartein, coniin, beta-eucain, gujasanol, physostigmin.

Oily: quinolin, alypin, lobelin.

Coca alkaloids give an oily residue if in small amounts, but if in quantity the cocain crystallizes in the mass.

Amorphous: antipyrin, brucin, sanguinarin, yohimbin. Hard, colorless, resinous mass: quinin.

Odor: Tobacco-like, nicotin, lobelin (also suggestive of honey).

A portion diluted with a little water: Mousy odor, coniin.

Guaiacol-like, gujasanol.

Pungent odor: spartein. Slight benzaldehyde-like quinolin.

Test for alkaloid: Dissolve the residue in petroleum ether, remove 5 drops, place on watch-glass and evaporate. Dissolve in 1 to 2 drops N/1 sulphuric acid, and add Mayer's reagent. A precipitate indicates an alkaloid. Note the color of this precipitate. If the solution in sulphuric acid is red, and a red precipitate is obtained, sanguinarin is indicated.

Physiological test: Evaporate 10 drops petroleum ether solution on a watch-glass, concentrating as much as possible in the center of the glass. If aconitin is suspected, perform the test very carefully. Remove a bit

on the end of a glass rod and apply it to the end of tongue, rubbing it with the rod. Tingling after one to five minutes indicates aconitin. Bitter indicates strychnin and quinin. Numbness at once, or after a few minutes, indicates cocain, beta-eucain, tropacocain, acoin, gujasanol, holocain, novocain, stovain. Anesthesia is not always obtained with such small quantities, and if no tingling is experienced, indicating aconitin, remove a larger quantity on the end of the finger and rub it thoroughly over the end of the tongue. If no sensation of numbness becomes apparent after five minutes it is doubtful if any of the anesthetics are present. If the residue was oily, evaporate 10 drops petroleum ether solution, and treat with 5 to 10 drops water. Physostigmin will dissolve quite readily. Apply a few drops of this solution to the eye of some animal having a normally large pupil, and note whether there is any contraction indicating physostigmin.

Evaporate 5 drops of petroleum ether solution in a porcelain dish and treat residue with 2 drops sulphuric acid. A red color indicates lobelin and sanguinarin. Then rub in a few pure crystals of potassium bichromate. Purple color indicates strychnin, yohimbin, Gelsemium bases. If coniin is present, an odor of butyric acid will be noted. The change of color in the case of strychnin is purple to cherry-red, gradually fading. Yohimbin gives a purple, but no change like strychnin.

Evaporate 5 drops of petroleum ether solution in a porcelain dish, and treat residue with 5 drops concentrated nitric acid. Red color indicates brucin, acoin.

Purple-red to dirty yellow indicates Gelsemium bases.

Orange color indicates sanguinarin, lobelin.

Yellow soon turning orange, physostigmin.

Now evaporate over the steam-bath (if any antipyrin is present the mixture will become deep purple on heating with nitric acid), and after the acid is entirely dissipated, as determined by the odor, cool the dish and add 5 to 10 drops alcoholic potassium hydroxide, noting carefully the odor, and, at the same time, the color produced. An agreeable odor of ethyl benzoate indicates cocain, aconitin, tropacocain, stovain. The odor should always be compared with that given by a known residue until the operator is familiar with it. In the case of stovain, the odor of isonitrile is also present. A purple color indicates antipyrin, strychnin, yohimbin, atropin. A red color indicates holocain.

If no odor develops in the cold, warm slightly over the steam-bath. Acoin also gives an agreeable odor, but not that of ethyl benzoate. Alypin, holocain and novocain give disagreeable odors.

Evaporate 5 drops in a porcelain dish and add 2 drops formaldehyde-sulphuric acid.

A crimson color gradually becoming purple indicates peronin. Repeat, using Froehde's solution, and the following color-reactions will be obtained in the presence of peronin: blue, deep violet, soon fading to dirty brown, then green, and finally slate color.

Cocain can be distinguished from tropacocain by heating the residue with dilute hydrochloric acid and salicylic acid in a pressure flask over the steam-bath for an hour. Cocain under these conditions will yield methyl salicylate which will be apparent on opening the flask and smelling the vapor.

Beta eucain gives a crystalline precipitate with pla-

tinic chloride which has a characteristic form under the microscope. The precipitate with gold chloride is amorphous. Alypin gives violet crystals with potassium, permanganate, which turn brown on standing. When alypin and stovain are warmed on the steam-bath with concentrated sulphuric acid and then treated with a little water, the odor of ethyl benzoate is evolved. Stovain base is thrown out of an acid solution by sodium bicarbonate; alypin and novocain are not. When a small quantity of novocain is treated with 5 c.c. of water, 2 drops of hydrochloric acid and 1 to 2 drops of sodium nitrite, and then added to a solution of beta naphthol, a scarlet precipitate is obtained.

Lobelin is volatile at the temperature of the steam-bath and can thus be distinguished from sanguinarin. Lobelin yields benzoic acid when warmed with 10 per cent alkali containing 4 per cent permanganate. On acidifying and shaking out with the ether the acid can be recovered.

Coniin and nicotin are volatile, and may be separated from the others of this group by boiling in a current of steam. The distillate should be cooled and then shaken out with petroleum ether and the solvent filtered and evaporated. A portion of this residue on treatment with silver nitrate solution will act as follows: free coniin gives a brown precipitate of silver oxide, which afterward becomes black. Nicotin gives a white precipitate, turning dark on exposure to light.

A solution of the residue or of a neutralized acid solution of the residue, with mercuric chloride gives a white amorphous precipitate with coniin, and a crystalline precipitate with nicotin, both readily soluble in hydro-

chloric acid or acetic acid. Nicotin and strychnin are the only alkaloids giving crystalline precipitates with mercuric chloride. Of course if the residue had been obtained by distillation no strychnin would be present.

A solution of the residue in dilute hydrochloric acid treated with platinic chloride solution gives a crystalline precipitate with nicotin. Coniin does not give a precipitate unless very concentrated. The platinic chloride compound of nicotin melts at about 275° darkening at 250°. This should be confirmed with a sample of a known product.

A solution of the residue in dilute hydrochloric acid treated with picric acid solution gives a precipitate with nicotin, but not with coniin, except in very concentrated solution. Nicotin picrate forms prisms melting at 218°.

Spartein: Three parts of iodin added to an ethereal solution of one part spartein gives a black precipitate. On separating and dissolving in boiling alcohol, green crystalline needles separate on cooling.

A solution of spartein in ether to which a few milligrams of sulphur are added, yields a bright-red precipitate when hydrogen sulphide is passed through the mixture.

There are a number of alkaloids which appear in small amounts in this fraction, while the greater portion will be extracted subsequently by ether and chloroform, and confirmatory tests will give better results when performed on these fractions. This applies to atropin, aconitin, brucin, emetin, holocain, physostigmin, quinin, sanguinarin, strychnin, and yohimbin.

In order to purify a residue, dissolve in dilute hydrochloric acid and precipitate with iodin in potassium

iodide. Filter and wash with iodin solution. Dissolve the precipitate in sulphurous acid, pour into separator, add ammonia in excess, and shake out with petroleum ether, wash, filter solvent into beaker and evaporate, which will give a residue of pure alkaloid.

Microchemical tests: Most of the alkaloids give, with certain reagents, precipitates having characteristic forms. This test is most valuable for confirming the identity of an individual. A check should be carried out at the same time with a known sample, until the analyst is familiar with the reactions. The preliminary tests with the color-producing reagents will indicate the alkaloid to be tested for. Cocain gives very characteristic precipitates with gold chloride, palladium chloride, potassium permanganate, picric acid; and several of the other anesthetics give characteristic tests. Strychnin gives a number of characteristic crystalline precipitates, and the opium bases appearing in subsequent fractions yield characteristic forms.

In making these tests it is desirable to have the alkaloids in a hydrochloric acid solution diluted from 1 : 100 to 1 : 200. The reagents giving the greatest satisfaction include N/10 iodin, 10 per cent platinic chloride, 5 per cent palladous chloride, gold chloride, picric acid potassium permanganate, potassium chromate, and chromic acid. A drop of the solution to be tested is transferred to a microscopic slide, the instrument adjusted and then a drop of the reagent added and the observation made. It will be necessary in some cases to start the crystallization by stirring the liquid with a glass rod. Another procedure consists in transferring a bit of the alkaloidal residue to a slide by means of a

needle or glass rod, dissolving it in a drop of dilute hydrochloric acid and then adding the reagent.

Now shake out three times with ether; if ether solution is green, it indicates apomorphin. Wash the combined solvents with water, filter into a beaker, and evaporate over a steam-bath, using a fan. The following substances will be removed:

Acoin base
Aconitin
Adrenalin, slightly
Anesthesin, 89–91°
Antipyrin, 112–113°
Apocodein
Apomorphin, partly
Atisin from Aconitum heterophyllum
Aspidospermin
Arecolin
Atropin, 112–113°
Berberin
Boldin
Brucin, 178°
Carpain
Cephaelin, 130°
Cevadin
Chelidonin, slightly
Cinchonamin
Cinchonidin, trace, 200–207°
Cinchonin, trace, 240–250°
Coca bases not readily soluble in petroleum ether
Codein, 154–155°
Conessin (Wrightin)
Corydalin
Cuprein, 198°
Cytisin, 152°
Delphinin, 119°
Dionin base, 110–115°, decomposes without melting
Emetin
Ephedrin
Ergotinin
Euquinin
Geissospermin, 160°
Gelsemin, 178°
Gelseminin
Harmalin, 238°, with decomposition
Harmin, 256–257°
Heroin, trace, 171°
Holocain base, 121°
Homatropin, 98–99°
Homoarecolin
Homochelidonin, 135–136°
Hydrastin, 132°
Hydrocotarnin
Hydroquebrachin
Hydroxyquinolin, 75–76°
Hyoscyamin, 106–108°
Jaborin
Jervin, trace
Laudanin, slightly
Laudanosin
Lobelin
Methylene Blue
Novocain, 51–60°
Nupharin

Orthoform, 141–143°
Oxyacanthin, 210°
Oxyspartein, 84°
Papaverin, 147°
Pereirin
Pelletierin
Peronin base
Physostigmin, 86–87° (dimorphous, 105–106°)
Pilocarpin
Pseudaconitin from Aconitum ferox
Pseudopelletierin
Psychotrin, 138°, partly
Quebrachamin, 142°
Quebrachin, 214–216°
Quinidin, sparingly, 168–170°
Quinin, 171–172°, anhyd.
Quinolin
Rubijervin, trace
Sabadin
Sabadinin, trace
Scopolamin, 59°
Sanguinarin
Strychnin, 265–269°
Thebain, 193°
Tritopin, 182°
Tropin, 61°
Veratralbin
Veratridin
Yohimbin, partly

Some of the reactions obtained with the petroleum ether residue will suggest what to expect in this fraction.

If acoin, aconitin, atropin, holocain, physostigmin, quinin, strychnin, sanguinarin, and yohimbin were suspected in the former, they will be found in larger quantities provided they were present in appreciable amounts in the original material. If the solvent, which was at first green, gradually assumes a magenta shade, the presence of apomorphin is strongly indicated.

A blue-colored residue indicates methylene blue, this being the fraction where it appears in marked quantity.

A colorless, hard varnish-like mass, with here and there a crystalline form appearing, indicates quinin.

Quinolin, pilocarpin and arecolin give liquid or oily residues.

Dissolve the residue in ether and evaporate 3 to 5 drops on a watch-glass. Dissolve in 2 to 4 drops dilute sulphuric acid, warming, if necessary, and to the solution add a drop of Mayer's reagent. A precipitate shows

that alkaloidal substances are present. A red precipitate indicates sanguinarin. A yellow oily precipitate soon crystallizing indicates arecolin.

Evaporate 5 drops on a watch-glass, and touch end of tongue to residue, very cautiously at first, and if aconitin was indicated in the previous fraction, the test had better be omitted, as a much larger quantity might appear at this point, and this alkaloid is extremely poisonous. If anesthesia is obtained, anesthetics are present. This should be thoroughly established, however, for unless one is familiar with the effect, the action of quinin is deceptive.

Evaporate in a porcelain dish. Add 2 drops concentrated sulphuric acid, and note the color; colorless, with blue color gradually developing, quebrachin. Blue indicates geissospermin. Red indicates sanguinarin and lobelin. Pale violet, soon fading, indicates papaverin. Yellow or orange, changing to violet, chelidonin. Rose pink, intensified by nitric acid vapors, indicates homochelidonin. Greenish fluorescent solution indicates harmin. Yellow to orange, indicates physostigmin (a crystal of potassium iodate produces a purple tint changing to yellowish red). Yellow with green fluorescence becoming pale red finally with a purple tint, most noticeable on rotating or tipping the dish, indicates sabadin, the combined Sabadilla alkaloids, commercial veratrin, and veratralbin from Veratrum. Yellow indicates hydroxyquinolin. Yellow soon becoming blood-red, pink on edges, and then bright red to pinkish red, indicates sabadinin. Yellow, on heating green and finally purple, pelletierin. Yellow to purple-red, atisin. Yellow with blue fluorescence more notice-

able on dilution indicates quinin and euquinin. Yellow, brown, greenish brown, finally green, jervin and pseudojervin; yellow, brown, red brown, purplish, rubijervin; if the red brown liquid is diluted with water, the color changes to crimson and passes through violet, purple to deep blue. Green, blue, violet protoveratrin. Red or brown gradually changing to pink and on warming purple and chocolate indicates mixed Gelsemium bases. Colors are obtained with other alkaloids, but nothing especially characteristic. If no color reaction is obtained, add small crystal bichromate and rub it around the acid with a glass rod. Purple to cherry-red indicates strychnin; purple to green or bluish green indicates yohimbin and gelseminin. Blue to brown indicates quebrachin. If a butyric odor develops during this reaction the presence of the Veratrum alkaloids is indicated.

Evaporate 5 drops in a porcelain dish. Add 2 drops concentrated nitric acid and note the color. Red indicates brucin or acoin. Orange indicates sanguinarin. Purple-red to dirty yellow, changing to dark green or bluish green indicates Gelsemium bases. Purple-red indicates geissospermin, disappears on heating. Yellow, soon turning orange, physostigmin. Blue to red indicates orthoform. Violet to deep mahogany-brown, finally orange, indicates apomorphin. Yellow, gradually green indicates heroin. Yellow solution with crystals orange-red until dissolved indicates codein. Pink rapidly disappearing is given by the mixed Sabadilla alkaloids (commercial veratrin). Now evaporate the acid over the steam-bath and note the residue. A blood-red residue, becoming deep green, is given by physostigmin. Blue-green residue indicates gelsemin. Red residues

are given by brucin and sanguinarin. Violet on heating is given by antipyrin.

When the residue is cool add 2 to 4 drops strong alcoholic potash, and note the odor and color. Aconitin gives a strong odor of ethyl benzoate. Agreeable odors, differing from ethyl benzoate, are given by some of the anesthetics, acoin, subcutin, while disagreeable odors are given by euphthalmin. The cinnamyl bases of coca leaves give an aromatic odor of cinnamic esters. Orthoform gives no odor. Purple color indicates atropin, hyoscyamin, scopolamin, strychnin, yohimbin. Homatropin does not respond to this test. Red: Holocain, nirvanin, novocain, orthoform, subcutin (blood red). Pseudaconitin gives purplish red. The Veratrum or sabadilla alkaloids do not give a characteristic color at this point. With physostigmin a brownish-green solution is obtained, a purple color appearing momentarily in thin layers; on subsequently adding acetic acid, the solution becomes green. Brucin, if in any quantity, will interfere somewhat with the test.

Evaporate 5 drops in a porcelain dish and add 2 drops sulphuric acid, containing formaldehyde. Brilliant violet to purple indicates codein, heroin, dionin. Crimson to purple indicates peronin. Deep purple, greenish-blue underneath, gradually deep blue-black, indicates apomorphin. Purple, violet to crimson, indicates papaverin. Red-brown indicates thebain. Dirty black-brown with deep purple gradually developing indicates apocodein. Salmon gradually red-brown indicates subcutin. Blue fading to yellow indicates acoin.

Evaporate 5 drops in a porcelain dish, and add 2 drops Froehde's reagent. No color at first, and then

gradually blue indicates codein. Green, deep green, blue, indicates dionin. Purple gradually blue indicates papaverin. Brown, changing to violet, blue, green and yellow homo-chelidonin. Crimson purple gradually fading indicates heroin. Blue, dirty brown, blue, green-brown, deep purple, with olive shade underneath, noticed on tipping dish, indicates apocodein. Blue at moment of solution, deep violet, soon fading to dirty brownish green, gradually slate-blue, indicates peronin. Deep red brown indicates thebain. Yellow, red with violet tinge, indicates sabadinin. Carmine to dirty brown, sanguinarin. Yellow to dirty brown chelerythrin. Pale violet, gray-brown on standing, purplish with yellow on edges, indicates berberin. Violet changing to yellow and green on edges, oxyacanthin. Violet soon fading to brown indicates physostigmin. Green indicates quinin.

If physostigmin has been indicated, evaporate 5 to 10 drops of the ether solution in a porcelain dish and add 1 c.c. hot ammonia. Physostigmin will produce a yellowish-red solution. Evaporate on a water-bath, which will leave finally, on drying, a blue or blue-green residue, which dissolves in alcohol, giving a blue solution. Add excess of acetic acid, which produces a violet-red solution, fluorescent.

When an alcoholic solution of physostigmin is treated with an aqueous solution of barium hydroxide in a flask with about one-quarter its volume of air, a red color appears, changing to green and blue as more air is admitted. On diluting and shaking out with chloroform the blue color is removed, and may be shaken out of the chloroform with hydrochloric acid.

If sanguinarin is indicated, pour 5 to 10 c.c. of the ether solution into a small flask and pass in slowly hydrogen chloride gas. If sanguinarin is present, a bright red precipitate of the hydrochloride will appear.

Chelerythrin gives a red to violet with ammonium vanadate reagent. A solution of the base in strong alcohol treated with carbon bisulphide containing iodin, gives a ruby red periodide melting 225°. The aurochloride melts 223° with decomposition.

Chelidonin sprinkled onto a solution of guaiacol in concentrated sulphuric acid produces a carmine-red color. Vanadium sulphuric acid gives green turning to blue-green. Gold chloride produces an orange-red precipitate which crystallizes violet-red from alcohol. The platinochloride is yellow and melts 155°.

Homochelidonin gives a blood red aurochloride which crystallizes from alcohol in warty crystals, melting 187°.

Bluish-purple shade changing to intense blue on adding hydrochloric acid is given by the mixed ipecac bases, Dirty green color changing to grass green on addition of hydrochloric acid indicates emetin.

Adrenalin is slightly soluble in ether. A neutralized solution is oxidized by air to oxyadrenalin, and the latter is removed from ammoniacal solution by amyl alcohol, but not by ether, chloroform, or petroleum ether. It gives a bluish-green color with a very dilute solution of potassium ferricyanide, containing ferric chloride, and a blue color with ammoniacal solution of phosphomolybdic acid. A solution of adrenalin gives a rose color on addition of iodin, a red color with mercuric chloride, and a reddish-violet with potassium biiodate and phosphoric acid and the same color with iodic acid. A solu-

tion of adrenalin (1 : 100,000) treated with an equal volume of 1 per cent sodium nitrate, and then with a few drops of mercuric chloride (1 : 1000), and warmed to 40 to 50°, gives a rose-red color. Potassium persulphate gives a characteristic red color. These color tests are given by bases closely allied to adrenalin, the aminobase corresponding to adrenalin, dihydroxyphenylethylamine, the corresponding methyl, ethyl, and propyl bases, and aminoacetopyrogallol.

If quinidin is suspected, a portion of the residue dissolved in hydrochloric acid is just neutralized and treated with a few drops of potassium iodide when a copious granular precipitation will take place if quinidin is present. The solution can then be tested further for quinin by filtering, adding ammonia and shaking out with ether. Cinchonidin will give a curdy precipitate with potassium iodide.

Potassium ferrocyanide gives a white flocculent precipitate with a solution of quinidin, a reddish-brown color with quinin and a white precipitate soluble in excess with cinchonin and cinchonidin.

Quinin may be substantiated by the thalleioquin and herapathite tests. Euquinin gives the thalleioquin, but not the herapathite test. Cuprein gives the thalleioquin test.

A small quantity of quinin dissolved in 2 c.c. concentrated sulphuric acid and treated with 0.5 c.c. hydrogen peroxide gives an intense yellow color on shaking. Quinidin gives the same reaction but the yellow color fades more rapidly than in the case of quinin.

The thalleioquin test is not easy to obtain unless the alkaloid is in considerable quantity, but the following

modifications will be of assistance: Saturated bromin water is added drop by drop until the fluorescence disappears, followed by 10 c.c. alcohol, and then 1 to 2 drops of ammonia; a green color should appear, following the addition of the ammonia, but in dilute solutions it will be very faint; on shaking with chloroform, the green color will be taken up by the solvent and brought into prominence. Salts of quinin should be dissolved in alcohol, and diluted with an equal volume of water before testing. Another modification consists in treating 10 c.c. of a faintly acid aqueous solution with 1 drop of a mixture of equal parts saturated bromin water and water, followed by one drop 10 per cent potassium ferrocyanide, and the same amount of 10 per cent ammonia water, and on shaking with chloroform a rose color is removed by the solvent.

The herapathite test is obtained by dissolving the residue in about 20 times its weight of acetic acid, adding half the volume of alcohol and a drop or two of dilute sulphuric acid and the mixture heated to boiling. A volume of saturated solution of iodin in alcohol equal to the amount of alcohol already present, is added and the mixture allowed to cool when the herapathite (quinin iodosulphate) will gradually separate. The crystals are black or bronze with iridescence. The quinidin compound is reddish brown and much more soluble so that it takes considerable time to precipitate. The iodosulphates of cinchonin and cinchonidin are also brown.

Euquinin has very little taste, it fluoresces with acids, and gives the thalleioquin test and when warmed with sodium hydroxide and iodin yields iodoform.

Cuprein in alcoholic solution gives a reddish-brown

color with ferric chloride. The base can be removed by ether from a solution made alkaline with ammonia, but if caustic alkali is used instead, it is not removed, differing thereby from the well-known Cinchona bases.

Separation of the Principal Cinchona Bases

Dissolve the residue in dilute sulphuric acid, exactly neutralize with sodium hydroxide, add an excess of saturated solution of Rochelle salt and let stand in a cool place for one hour, stirring from time to time. A precipitate occurs if cinchonidin is present. Filter, concentrate, cool, add a drop of acetic acid and an excess of a saturated solution of potassium iodide. Stir from time to time for two hours in the cold, and a granular precipitate comes out if quinidin is present. Filter, add ammonia and shake out with ether-chloroform, 3 : 1, separate solvent and evaporate. Dissolve in acetic acid and perform herapathite reaction exactly as described above, allowing to stand for twelve hours in case no immediate precipitate comes out. The formation of iridescent bronze or black crystals shows quinin. Filter, destroy excess of iodin by means of sulphurous acid, evaporate off alcohol, dilute with water, add ammonia, shake out with chloroform, separate and evaporate the solvent. Dissolve the residue in dilute sulphuric acid, neutralize, and add potassium ferrocyanide drop by drop, a white precipitate soluble in excess shows the presence of cinchonin.

If it is desired to recover the bases, the individual fractions thus obtained can be transferred to separators, treated with alcohol and ammonia, diluted with water

and shaken out with ether, or ether-chloroform. The residues can then be dissolved in dilute hydrochloric acid, precipitated with picric acid, the picrates filtered off, recrystallized, dried and their melting-points determined.

Quinin picrate melts 125–126°.

Quinidin picrate melts 137–138°.

Cinchonin picrate melts 193–194°.

Cinchonidin picrate melts 208–209° (darkens 200°).

The fluorescence of the solutions of cinchona alkaloids has been found to vary; thus when 0.02 gram is dissolved in 2 c.c. glacial acetic acid and 2 c.c. concentrated sulphuric acid, a slight fluorescence is noted with quinin, cuprein, cinchonin, and cinchonidin; on adding 0.02 c.c. formaldehyde a strong bluish fluorescence is noted with quinin and cuprein, with cinchonin blue, and cinchonidin bluish-violet; on adding 3 to 4 c.c. water the fluorescence of the cuprein disappears and the green of the quinin is accentuated; on further dilution with water the fluorescence of cinchonidin disappears rapidly, and is barely visible at 10 to 15 c.c., while it is evident up to 50 c.c. with quinin, and stronger still with cinchonin.

Gelsemin.—The precipitates formed with gold or platinum chloride are yellow, soluble in hot water, and precipitating in crystalline form on cooling. The pure alkaloid dissolves in nitric acid to a colorless solution, and on evaporating spontaneously a permanent blue-green color is obtained. As usually obtained, gelsemin residues give with nitric acid yellowish to brownish-green colorations, rapidly changing to deep green or blue green. Sulphuric acid and bichromate give reddish purple to cherry-red, rapidly changing to bluish-green or blue tint. Sulphuric

acid containing other oxidizing agents produces varying shades of magenta or purplish red.

Gelseminin.—Sulphuric acid gives a yellow, changing to violet with bichromate, and finally green. Its solution causes dilation of the pupil. These bases give no characteristic color with formaldehyde-sulphuric acid.

Ipecac Alkaloids: *Emetin—Cephaelin—Psychotrin.*—A drop of solution of calcium hypochlorite applied to a fragment of the solid substance, and a drop of acetic acid added, gives a very persistent bright orange or lemon-yellow color. If the solution of calcium hypochlorite is added to a solution of the alkaloids in dilute hydrochloric acid, an orange coloration is produced, and a yellow precipitate formed. A neutralized solution of the alkaloids in hydrochloric acid gives a blue color with ferric chloride, later changing to green. They give blue color with starch and iodic acid, and yield Prussian blue with ferric chloride and potassium ferricyanide. The residue does not give a characteristic color with formaldehyde-sulphuric acid.

Cephaelin can be separated from emetin by dissolving the mixed bases in hydrochloric acid, adding a slight excess of caustic alkali and shaking out with ether. The ether solution, after separating, is shaken with dilute alkali, and the latter, after washing with ether, is added to the original aqueous solution which should now contain all of the cephaelin, the emetin being in the ether, and may be obtained on evaporation. To recover the cephaelin, the alkaline liquid is treated with a slight excess of hydrochloric acid, then made ammoniacal and shaken out with ether-chloroform mixture (1 : 6).

Emetin neutralized with dilute hydrochloric acid and

boiled with a little ferric chloride gives rubremetin hydrochloride, a scarlet substance soluble in chloroform. Emetin when warmed on the steam-bath with benzoic anhydride yields benzoyl emetin. The cooled melt is dissolved in ether, the benzoyl emetin shaken out with dilute sulphuric acid, the acid separated, treated with ammonia and shaken out with ether. On evaporating the ether the benzoyl emetin will be left and may be crystallized out of absolute alcohol. It melts 185–186°.

Pelletierin is soluble in 20 parts cold water. Ammonia produces a white precipitate soluble in excess, giving a yellowish-red solution.

Pilocarpin is readily soluble in water. Its solutions are dextrorotatory, neutral to litmus, but alkaline to cochineal. No precipitates are formed with tannin, picric acid, or potassium ferrocyanide. The precipitate with gold chloride containing 1 molecule of water melts at 100°, the anhydrous salt at 138°. If .01–0.02 gram of a salt of pilocarpin is dissolved in 2 c.c. water, 2 c.c. slightly acid solution hydrogen peroxide added with 2 c.c. benzol and 3 to 4 drops bichromate solution 1 : 300, and the mixture gently shaken, the benzol will acquire a violet color, blue if the quantity is considerable, while the aqueous layer remains yellow.

In connection with the above test for pilocarpin it should be noted that pyridin and quinolin both give a violet color under the same conditions but the color soon fades; apomorphin gives a violet changing to green on separating the benzol and adding dilute stannous chloride; antipyrin gives a blue color, distinguishable from that of pilocarpin by shaking the benzol layer with water containing a trace of hydrochloric or sulphuric

acid, and treating this acid layer as before with peroxide, bichromate, and benzol, when the color will be regenerated, which is not the case with pilocarpin.

Pilocarpidin is not precipitated from aqueous solution by gold chloride. The compound with platinum chloride melts at 186–190°.

Strychnin and Brucin.—The presence of strychnin will be apparent in the petroleum ether fraction and if brucin is present in the sample, not enough will be extracted by petroleum ether to interfere with the strychnin reactions. In the ether and chloroform fractions brucin will interfere with oxidation tests.

The color tests given by strychnin with oxidizing agents and a nitric acid residue with alcoholic potash have been noted. The alkaloid forms a large number of crystalline salts with some of the usual precipitating reagents and many of these have characteristic forms when viewed under the microscope. It differs in this respect markedly from yohimbin, which though it might be mistaken for strychnin from its color tests, gives very few crystalline salts.

Strychnin can be separated from brucin by dissolving the residue in 15 c.c. 3 per cent sulphuric acid, adding 3 c.c. of a cool mixture of equal parts concentrated nitric acid and water, stirring occasionally for ten to fifteen minutes, transferring to a separator, adding excess of sodium hydroxide and shaking out with chloroform, which removes the strychnin. By this method the brucin is lost, and if it is desired to reserve the brucin, the residue is dissolved in 15 c.c. dilute sulphuric acid, diluted with 100 c.c. water, 25 c.c. 5 per cent potassium ferrocyanide added and the mixture well shaken and allowed to stand six

hours. After filtering, the filtrate is treated with excess of ammonia and the brucin shaken out with chloroform.

Brucin gives a scarlet or blood-red color with nitric acid, which on heating changes to yellowish red and finally yellow. On adding a few drops of a freshly prepared dilute stannous chloride solution, an intense violet color appears, which changes to yellow or red on heating, and again reappears on the addition of more stannous chloride. The reddish or deep-orange color produced by adding nitric acid to morphin remains unchanged by stannous chloride.

The ferricyanide and hydrochlorplatinate are characteristic compounds showing well-developed forms under the microscope.

Yohimbin reacts as follows: On adding sulphuric acid, a yellow color is obtained which with potassium dichromate gives a purple color changing to blue, red, and finally green; if the amount is large, the first color is indigo-blue, changing rapidly to olive-green. Nitric acid forms a yellow solution which becomes orange on evaporation; alcoholic alkali produces a purple color momentarily, then chocolate, and on warming the residue turns almost black; as the last portion of alcohol evaporates there is an odor of orange flower.

Codein and dionin give similar reactions in almost all cases, but with a 10 per cent solution of codein hydrochloride a precipitate appears on the addition of a few drops of ammonia, which dissolves on the addition of 1 c.c. ammonia, while dionin requires the addition of 5 c.c. ammonia and soon separates on standing, this fact being characteristic with a 1 per cent solution of dionin. When

the base of dionin is dissolved in water and ferrichloride containing a trace of ferricyanide is added, a blue-green color develops. Codein does not give this reaction. Codein is soluble in warm water and in ammoniacal water. The aqueous solution does not reduce iodic acid, nor give a blue color with ferric chloride. Codein picrate, recrystallized from 10 per cent acetic acid, melts 195.5–196.5°.

Aspidospermin with sulphuric acid and lead peroxide gives a brown color changing to purple-red. On boiling with perchloric acid an intense red color results; it is claimed that this reaction is not given when the acid is pure, but only when impurities having oxidizing power are present. Platinic chloride gives a blue precipitate which becomes violet on boiling with excess of the reagent. It forms a yellow chromate which turns green on exposure to air.

Hydroquebrachin gives a violet color with sulphuric acid, and the same reaction with perchloric acid as aspidospermin. The chloroplatinate is yellow, and dissolves in boiling hydrochloric acid, with a brown-red color, depositing a blue precipitate on standing.

Quebrachin gives a bluish solution with sulphuric acid, turning to blue and brown with dichromate. With perchloric acid the color is yellow.

Quebrachamin gives a violet color with sulphuric acid and bichromate, and a yellow to yellowish red with perchloric acid.

Aspidospermatin gives with perchloric acid the same color as aspidospermin, but the precipitate with platinic chloride is yellow.

Aspidosamin gives with sulphuric acid a brown color,

COLOR REACTIONS OF LOCAL ANESTHETICS

	Formaldehyde and Sulphuric Acid	Molybdic Acid and H_2SO_4	Selenous Acid and H_2SO_4	Bichromate and H_2SO_4	Phospho-Molybdic Acid	Phospho-Tungstic Acid	Potassium Chromate	Same and Equal Volume HCl	Tannic Acid	Nitric Acid	Nitric Acid to Dryness	Same, with addition of Alcoholic KOH	Wagner's Reagent	Mayer's Reagent	Ferric Chloride	Ferric Chloride to Neutral Solution	Potassium Permanganate	A. Bromine Water B. After addition of ammonia
Acoin 176°	Blue, fading to yellow.	Olive-green, changing to brown-yellow, rim changing to blue and finally green.	Golden yellow, dark brown to olive green.	Reduction to green.	Cream white precipitate.	Flesh-colored precipitate.	Yellow curdy precipitate.	Precipitate resinifies; dirty red color. Develops in solution.	White precipitate.	Strong red.	Deep red.	Agreeable odor.	Red-brown precipitate.	Curdy white precipitate.			Immediate reduction. Precipitate dissolves.	A. Dirty yellow curdy precipitate. B. Purple precipitate sol. in NH_4OH
Alypin 169°				Slow reduction to green.	Yellow curdy precipitate.	White curdy precipitate.	No precipitate.					Disagreeable odor.	Red-brown precipitate.	White precipitate.				A. —— B. White precipitate.
Anesthesin 89–91°	No color.	No reaction. At first faint blue on outer rim on standing.		Dirty purple. Slow reduction.	Cream precipitate.	White curdy precipitate.	No precipitate.	Brown precipitate, reduction.			Dark greenish-black.	No odor.	Red-brown precipitate.	No precipitate.			Immediate reduction, brown color	A. White precipitate. B. No change.
Beta-Eucain Mpt. 268°. Base liquid				Slow reduction.	Curdy white precipitate.	White curdy precipitate.	Yellow precipitate.	Yellow solution. No reduction.			No color change.	Agreeable odor, oily drops.	Red-brown precipitate.	White precipitate.				A. Yellow precipitate. B. White precipitate.
Euphthalmin		No color at first, blue on outer rim on standing.		Reduction to olive-green.	Yellow curdy precipitate.	White curdy precipitate.	No precipitate.				Slight yellow.	Benzaldehyde odor, red oily drops.	Red-brown precipitate.	White precipitate.				A. —— B. ——
Holocain Base 121°		Green, changing to blue.	Yellow.	Slow reduction.	Curdy white precipitate.	Light brown curdy precipitate.	Yellow precipitate.	Brown, changing to green.	White precipitate sol. in excess.	Yellow to brown.	Yellow.	Dark red color. Disagreeable odor.	Yellowish precipitate.	White precipitate.			Reduction.	A. Yellow milky precipitate. B. Brown-gray precipitate.
Nirvanin 185°		Prussian blue. Color fades.		Slow reduction. Pinkish green.	Cream white.	Flesh-colored curdy precipitate.	Yellow precipitate.	Precipitate dissolves, reduction.	White precipitate.	Yellow with green tinge.	Reddish.	Red color. No odor.	Red-brown precipitate.	White precipitate.		Intense purple color.	Immediate reduction.	A. Yellow precipitate. B. Sol. to yellow solution.
Novocain Mpt. 150–155°. Base 58–60° with $2H_2O$					Cream white	White curdy precipitate.	No precipitate.	Reduction to green on standing red.			Yellow-red.	Dark red color. Isonitrile odor.	Red-brown precipitate.	White precipitate.			Reduction to clear brown-red sol.	A. Bright yellow precipitate. B. White precipitate.
Orthoform 141–143°				Green to blue.	Precipitated with reduction.	Yellow precipitate.	Deep green.	Reduction to deep green.		Blue to red.	Red.	Red color. No odor.	No precipitate.	No precipitate.	Red color, brown precipitate.	Dirty green.	Reduction to green precipitate.	A. Yellow-green precipitate.
Stovain Mpt. 175°. Base.			Yellow, rose red on edge.	Reduction.	Yellow	White precipitate.	No precipitate.	Precipitated solution on excess of acid.				Ethyl benzoate with isonitrile.	Precipitate.	Precipitate.	Green.			A. Precipitate white. B. No change.
Subcutin 195–196°.	Salmon gradually, then red brown.				Yellowish - white precipitate.	White precipitate.	No precipitate.	Deep red to brown with brown precipitate.	No precipitate.		Brownish - yellow residue.	Blood-red color. Agreeable odor, not ethylbenzoate.	Precipitate with oily drops.	No precipitate.	Small amount produces a brown precipitate.		Green at once.	A. White precipitate. B. No change.
Propaesin Mpt. 74–76°	No reaction.	No reaction.		Green to dirty olive	Curdy white	White precipitate.	No precipitate.	Darkens, and precipitate soon comes out dirty brown.	No precipitate.	No reaction.	Brown-yellow.	No charact. odor. No color.	Chocolate - brown precipitate.	No precipitate.	No reaction.		Dilute permangan. is immediately decolorized, and when excess is added reduction.	A. White precipitate. B. No change.

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turning blue with dichromate. With perchloric acid a fuchsin-red color is obtained.

Hydroxyquinolin is volatile with steam. It has a saffron-like odor, and is soluble in acids and dilute alkalies with a yellow color. Its solution in absolute alcohol is colorless, but turns yellow on adding water. An aqueous solution gives a green color with ferric chloride and a red color followed by a black precipitate with ferrous sulphate.

Arecolin is soluble in water and volatile with steam, the aqueous solution being strongly alkaline. With potassium-bismuth iodide it gives a fine crystalline pomegranate red precipitate. Gold chloride gives a yellow oily precipitate. The acid solution is not precipitated by tannic acid, platinic or mercuric chlorides.

Cytisin gives a red color with ferric chloride. On adding hydrogen peroxide the color is destroyed and on warming the liquid a blue color is produced. Concentrated sulphuric acid gives no color with cytisin, but on adding thymol and warming a yellow to red is produced. Nitrobenzol containing a trace of nitrothiophen colors the alkaloid violet red. The aurochloride melts 212–213°.

Harmin forms colorless salts which show an indigo-blue fluorescence in aqueous solution. Harmalin forms yellow salts which show a blue fluorescence in aqueous solution, but the solution in concentrated sulphuric acid is not fluorescent. Harmalin, on boiling with hydrochloric acid, yields harmalol, a phenolic alkaloid, which crystallizes in red needles melting 212°. Harmalol gives a yellow fluorescent solution with water, the fluorescence being destroyed by acids and alkalies.

Ergotinin dissolved in concentrated sulphuric acid gives with a drop of ferric chloride an orange-red color, becoming deep red, with a blue to bluish-green margin. A solution in glacial acetic acid to which ferric chloride is added and carefully overlaid on concentrated sulphuric acid yields a violet zone at the point of contact.

The Sabadilla and some of the Veratrum alkaloids will appear in this fraction and the next. The Sabadilla bases produce intense sneezing and in addition to the color tests already noted give a blood-red color with hydrochloric acid. Sulphuric acid containing furfurol gives a dark-green color becoming violet on warming. Veratralbin occurs in Veratrum and gives reactions very much like those given by the Sabadilla bases. Protoveratrin gives a dark cherry-red color with hydrochloric and phosphoric acids. Jervin forms a very sparingly soluble hydrochloride and nitrate. The salts are best prepared by dissolving the base in acetic acid, avoiding an excess, and adding an alkali chloride or nitrate.

Some of the synthetic anesthetics, notably the bases of acoin, holocain, and orthoform " new," appear in this fraction. Acoin base dissolved in dilute hydrochloric acid, gives a yellow curdy precipitate with bromin water which turns pink on the addition of ammoniacal chloroform. Holocain base dissolved in a slight excess of hydrochloric acid gives a violet precipitate with calcium hypochlorite which is soluble in ether to a red solution. Orthoform dissolved in water to which a drop of sulphuric acid is added and treated with a few drops of sodium nitrite, gives a yellowish-red solution and a yellow precipitate which turns red in contact with air.

The mydriatic alkaloids will be found in this and the

subsequent fraction. If indicated by the reaction with nitric acid and alcoholic potash, dilute solutions of the base in hydrochloric acid should be treated on the microscopic slide with gold chloride and with picric acid, comparing the form of the crystals produced with those given by known specimens. Atropin gives a very characteristic crystalline precipitate, with a saturated solution of bromin in hydrobromic acid. The aurochlorides, recrystallized out of hot dilute hydrochloric acid and dried at 80°, and the picrates recrystallized out of dilute acetane have sharply defined melting-points.

	Atropin	Hyoscyamin	Scopolamin	Homatropin
Aurochloride	135°	160–162°	198–199°	142–145°
Picrate	174–175°	161–164°	187–188°	180–181°

Separation of Strychnin and Quinin

Dissolve the residue in 5 c.c. alcohol-hydrochloric acid mixture (9 parts alcohol, 1 part dilute hydrochloric acid), add 20 per cent platinic chloride, drop by drop, agitating until precipitation is complete. Add 5 c.c. more of the solvent and let stand one hour and then filter. To the filtrate add excess of alkali and shake out quinin with ether. The precipitate is washed with the solvent, transferred to a separator, treated with ammonia and shaken out with chloroform which will dissolve the strychnin.

If brucin is present the residue must be subjected to a preliminary treatment with nitric acid as described above for separating that alkaloid from strychnin.

Now shake out three times with chloroform, wash the combined solvents with water, run chloroform through

cotton into a beaker. Note whether the solvent is fluorescent, denoting chelerythrin. Evaporate over the steam-bath, using a fan. The following substances will be removed:

Aconitin
Atropin, 112–113°
Apomorphin
Berberin, trace
Brucin, 178°
Celandin bases
Chelidonin, 135°
Cinchonin, 240–250°
Cinchonidin, 200–207°
Codein, 154–155°
Colocynth alkaloid
Cytisin
Delphinin
Heroin, 171°
Hydrastin, 132°
Hydroxyquinolin, 75–76°
Hyoscyamin, 106–108°
Isopelletierin
Jervin
Laudanin
Methylene Blue
Morphin, trace
Narcein, 145°, when anhyd.
Papaverin, 147°
Pelletierin
Physostigmin
Psychotrin, 138°
Protopin
Protoveratridin, trace
Protoveratrin, trace
Pseudojervin
Quebrachin, 214–216°
Quinidin, 168–170°
Rubijervin
Sabadinin
Sanguinarin
Strychnin, 265–269°
Scopolamin
Tritopin
Yohimbin

This fraction is in the main used for confirmatory tests for certain alkaloids which may have been indicated to a greater or less extent in the previous residues obtained from shaking out the alkaline solutions. Cinchonin, cinchonidin, yohimbin will appear at this point in quantities sufficient for their more ready detection than in the previous fraction. Morphin will be extracted in small quantity, and brucin and strychnin are removed by chloroform better than by any other solvent.

If atropin, hyoscyamin, scopolamin, codein, heroin, hydrastin, papaverin, physostigmin, sanguinarin, strychnin, or brucin have not been indicated on previous

occasions, there is little use of looking for them here. The same series of color reactions as was performed on the ether residue should be conducted here.

Morphin gives with nitric acid a red solution gradually fading, but this reaction is useless when brucin is present. With Froehde's reagent and with sulphuric acid and formaldehyde purple shades are obtained, but morphin is best identified in the next fraction.

Aconitin.—Dissolve residue in water containing a few drops acetic acid, and take 1 to 2 c.c. in the mouth, rolling it around with the tongue, and then expectorate. If aconitin is present, the peculiar tingling sensation will soon appear. If sufficient alkaloid is present, prepare the aurochloride, which is a well-defined crystalline salt, wash, dry, and take the melting-point, which, in the case of the pure salt, is 135°.

The crystalline precipitates given by aconitin with potassium permanganate and iodin have characteristic microscopic forms when viewed under the microscope.

Pseudoaconitin evaporated with nitric acid and the residue treated with alcoholic potash gives a purplish-red color. A similar color is produced when warmed with sulphuric acid. The aurochloride melts 236–238°. It forms a nitrate which is only slightly soluble in water and melts at 185–186°.

Atropin, hyoscyamin and scopolamin are indicated by the purple color given in the nitric acid-alcoholic potash reaction. If strychnin has been indicated by the oxidation reaction it must be separated, as it too gives a color test similar to the above-mentioned bases with nitric acid and alcoholic potash.

If strychnin has been found and it is desired to test

for atropin, hyoscyamin, or scopolamin, dissolve in dilute sulphuric acid, add potassium ferrocyanide, filter, add ammonia, and shake out with chloroform; on evaporation the residue will contain the Solanum bases free from strychnin, and they may be identified by the michrochemical tests and the melting-points of the aurochlorides and picrates.

Gold chloride throws out atropin from dilute acid solution as an amorphous or oily precipitate which gradually becomes crystalline and has a well-defined form under the microscope. It melts under hot water and is deposited from its solution in boiling water acidulated with hydrochloric acid in minute crystals which are lusterless after drying at 80° C. and melts 135–138°. Hyoscyamin aurochloride retains its luster when dry and melts 160–162°; scopolamin aurochloride melts 198-199° and homatropin aurochloride 142–145°.

The picrates of these alkaloids are thrown out of concentrated solutions in dilute hydrochloric acid, and after washing with water are recrystallized from dilute acetone. Atropin picrate melts 174–175°. Hyoscyamin picrate 161–164°. Scopolamin picrate 187–188°. Homatropin picrate 180–181–185°.

These crystalline salts when viewed under the microscope are valuable confirmatory tests.

Shake out three times with a mixture of chloroform and alcohol, 2 : 1, filter solvent, and evaporate over steam-bath, using fan. The following substances will be removed:

Berberin	Solanin
Narcein, 145°, when anhydrous	Salicin, 200–202°
Morphin, 254°, rapid heating	Strophanthin

Note whether residue is crystalline. Morphin, if present in sufficient quantity, will appear in crystalline condition. Note color: berberin will give a yellow residue.

Dissolve the residue in a mixture of chloroform-alcohol (2 : 1) or in alcohol.

Evaporate 1 to 2 drops on a watch-glass. Dissolve residue in 2 to 3 drops dilute sulphuric acid, and add Mayer's reagent. A precipitate shows the presence of an alkaloid.

Evaporate 2 to 4 drops in a porcelain dish and add 1 to 2 drops concentrated sulphuric acid. Red color indicates salicin. Deep brown at moment of solution, yellowish, gradually becoming green, and finally blue, indicates narcein. Orange, olive-green on warming, indicates berberin. Add a crystal of bichromate and note reaction. With berberin a violet shade, becoming brownish-green, will be observed. There are many descriptions of this reaction, probably due to the condition in which it occurs as extracted from the extract of the drug. A fragment of sodium nitrate stirred into a solution of berberin in concentrated sulphuric acid gives a violet streak.

Evaporate 2 to 4 drops in a porcelain dish, and add 1 to 2 drops concentrated nitric acid. Deep red, gradually fading, indicates morphin. Berberin gives a dark reddish-brown liquid, which, on dilution with water, gives a yellow precipitate partly soluble in ammonia.

Evaporate 2 to 4 drops in a porcelain dish and add 1 to 2 drops Froehde's reagent. Purple coloration is given by morphin and salicin; greenish brown fading indi-

COLOR REACTIONS OF THE OPIUM BASES AND DERIVATIVES AND OTHER ALKALOIDS.

	Froehde's.	Ammonium Vanadate.	Formaldehyde $+H_2SO_4$.	$K_2Cr_2O_7+H_2SO_4$.	H_2SO_4.	Nitric Acid.
Morphin....	Purple, fading to slate.	Yellow—faint violet—dirty brown—slate	Deep purple.	Greenish - gray — dirty green.		Deep red, gradually fades.
Codein.....	No color at first, gradually blue.	Pale green—gradually blue.	Deep purple.	Dirty green.		Yellow, crystals orange until dissolved.
Heroin.....	Crimson - purple, soon fading.	Pale violet, soon fading.	Crimson - purple, deepening.	Flesh color momentarily.		Pale yellow, gradually *green.*
Dionin.....	Gradually green—deep green—*blue.*	Gradually green.	Yellow - purple, deepening.	Greenish yellow.		Yellow.
Apomorphin.	Deep blue, fading to slaty-violet.	Deep blue.	Purple — greenish blue underneath, finally deep blue-black.	Deep green.		Violet, mahogany, brown, orange.
Peronin.....	Brown — violet — dirty brown-green—slate.	Olive brown.	Crimson gradually purplish tint.	Yellow-brown.		Yellow.
Narcotin....	Deep green.	Brick-red—pink in thin layers.	Purple to slate, soon fading.	Pink—brick-red—reddish yellow—pink in thin layers.	Pale yellow—pink on edges—red gradually develops.	Deep yellow.
Narcein.....	Green-brown, fades.	Reddish brown.	Brown, green on edges, gradually deepening.		Brown —yellow—green — finally blue.	Yellow fading.
Papaverin...	Purple, gradually blue.	Purple — blue — green—deep blue.	Purple — violet — crimson.	Purple— brown—finally purple.	Pale violet soon fading.	Yellow.
Thebain.....	Red-brown.	Red-brown.	Red-brown.	Red-brown.		Yellow.
Apocodein...	Blue—dirty brown—blue - green—purple—olive underneath.		Brown - black — brown—purple.			
Hydrastin...	No reaction at first, gradually deep green.	Pink—bright red—brick red.	No reaction.	Brown — pinkish-violet—brown.	No reaction.	Yellow.
Colchicin....	Yellow.	Yellowish green.	Crystals reddish, liquid yellow.	Green soon fading.		Deep purple.

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cates narcein; greenish brown to dark brown or violet indicates berberin.

Evaporate 2 to 4 drops in a porcelain dish and add 1 to 2 drops formaldehyde-sulphuric acid. Deep purple indicates morphin.

An aqueous solution of morphin, free from acid, gives a deep-blue green color with ferric chloride, changing to green as more of the reagent is added, and disappearing on adding acids. The aqueous solution gives a blue color or precipitate with ferric chloride and potassium ferricyanide. It also reduces iodic acid with liberation of iodin, and then if ammonia is added a mahogany color develops.

Morphin gives crystalline precipitates with iodin, palladous chloride and picrolonic acid, which are characteristic when viewed under the microscope. If a solution of morphin in concentrated sulphuric acid is warmed to 100° and treated with a drop of nitric acid, a chlorate or chlorin water, a blue to purplish color appears, passing to deep red and gradually fading.

Berberin is easily dissolved in warm water. The aqueous solution is precipitated by potassium iodide, not always immediately, but usually after several hours' standing. When a solution of berberin strongly acidified with hydrochloric acid or sulphuric acid is treated with a small quantity of chlorin water cautiously added from a pipette and allowed to rest on the surface of the liquid to be tested, a zone of bright red is formed at the junction of the two liquids.

Strophanthin is readily changed by mineral acids even in the cold to glucose and strophanthidin, or by heating

at 70° for one hour with dilute sulphuric acid. Strophanthidin is slightly soluble in cold water, but readily soluble in chloroform, and may be removed by shaking with this solvent.

An aqueous solution of strophanthin froths on shaking. It is not precipitated by neutral or basic lead acetate, but an aqueous solution of the drug gives a precipitate due to kombic acid; it is precipitated by tannin, the precipitate dissolving on agitation, until an excess is added. With phosphomolybdic acid the solution gives a green color, gradually changing to greenish blue. Pure strophanthin gives a green color with sulphuric acid, rapidly changing to greenish yellow and brownish green and in an hour or two becoming dirty brown without any green; when moistened with sulphuric acid, and heated to 50-60°, the green color becomes dark olive changing to very dark brown, then violet and dark violet-blue, and finally to black with violet tint. With dilute sulphuric acid, it gives a nearly colorless solution, developing various shades of green on heating to 50°, and changing to violet, and in about two hours to violet-black. Ten per cent nitric acid dissolves strophanthin without color; but on heating to 50° a violet color appears, changing gradually to yellowish brown, and finally to gamboge-yellow.

Salicin when subjected to hydrolysis with emulsin is hydrolyzed, saligenin and glucose result. The solution should be shaken out with ether, and the ether filtered and evaporated, which leaves the saligenin. An aqueous solution of this product is colored indigo-blue by ferric chloride. The residue is soluble in concentrated sulphuric acid with a bluish-red color. When boiled with

dilute mineral acids salicin yields saliretin, which on boiling with nitric and sulphuric acid is converted to picric acid.

STILL IN SOLUTION

Adonidin	Phenolsulphonic acid
Arbutin	Polygalic acid
Aloin	Protoveratrin
Convallamarin	Protoveratridin
Digitalis glucosides (Digitalin and Digitonin)	Senegin (Senega saponin)
Gentiamarin	Saponins
Glycerin	Sapotoxin
Helleborein	Sarcosin
Hexamethylenetetramin	Sozolic Acid (Orthophenolsulphonic)
Narcein	Tannic acid

(Salts soluble both in water and alcohol: see table No. 1, page 6.)

From the table above it will be noted that there are a number of fairly common organic substances which are not removed by the regular group solvents. In certain instances it will be found difficult to identify their presence with any degree of certainty, though often, if the possibility of an individual is suspected, it may be substantiated by taking a fresh portion of the original sample and making special tests for the substances.

The solution should be neutralized and small quantities (2–5 c.c.) tested with following reagents:

Add solution of tannic acid (gallotannic acid, pure crystals) and note whether a precipitate occurs at once or on standing several hours. The Digitalis glucosides, adonidin, helleborein, and convallamarin are thrown out, but arbutin and gentian glucosides are not precipitated.

To another portion add a slight excess of hydrochloric

acid followed by Mayer's reagent, which will give a copious precipitate if hexamethyleneamine is present.

To another portion add a slight excess of hydrochloric acid, heat nearly to boiling and add barium chloride drop by drop until no further precipitation takes place, then add a few drops in excess. Filter. To filtrate add 5 c.c. bromin water and heat to boiling. A precipitate of barium sulphate and tribromphenol occurs if phenolsulphonic acids are present.

Treat 10 mils of the solution with a slight excess of hydrochloric acid, saturate with sodium chloride and shake out with ethyl acetate. Separate ethyl acetate, wash with saturated solution of sodium chloride, let stand half an hour, separate, evaporate the ethyl acetate, dissolve residue in water and test with ferric chloride. A black or greenish-black color is given by tannins.

Saponins, if present, will have been indicated by the frothing of the solution during the shaking out with immiscible solvents, and perhaps by the formation of emulsions which have separated with difficulty.

The character of the substances still in solution as indicated by these preliminary tests will determine how much of the solution can be used for the subsequent examination.

If glucosides are indicated treat the neutralized liquid with solution of tannic acid and allow it to stand until the precipitate of glucoside-tannin compound has settled out. Decant the solution through a filter and wash precipitate. To the filtrate add a slight excess of hydrochloric acid, saturate with sodium chloride and shake out several times with ethyl acetate. Combine the solvent solutions, wash with saturated sodium chloride, let stand,

separate, and evaporate. The residue will contain tannic acid, arbutin, and the gentian glucosides. Treat the residue with warm water, filter if necessary and add lead oxide (litharge) and agitate until the tannin is precipitated. Filter, acidulate with hydrochloric acid, shake out with ethyl acetate as before, separate and evaporate the solvent.

Arbutin dissolved in water gives a fine blue color with ferric chloride. Arbutin gives a blue tint when treated with a solution of sodium phosphomolybdate in hydrochloric acid followed by a slight excess of ammonia. A 1 per cent solution reduces ammoniacal silver nitrate on boiling, and gives a precipitate with sodium hypobromite. On boiling with dilute acids, quinol or hydroquinone is formed; the latter is readily removed from acid solution by ether, and its production under these conditions indicates the presence of arbutin; it may be identified by its melting-point, 169°, sublimation on heating, its precipitating Fehling's and ammoniacal silver nitrate solutions, and the sodium hypobromite color reaction.

The Gentian Glucosides.—Gentian may be dried in the air under cover without losing much gentiopicrin, but this glucoside is usually in small amount in the commercial drug; it is also hydrolyzed by alcohol, and the ordinary medicinal preparations are therefore free from it. Gentiopicrin is soluble in ethyl acetate, and the crystals have a melting-point 189°, and a strong levorotation; gentiogenin is produced on hydrolysis, and gives with sulphuric acid a brown color, changing to blue with water. If dissolved in 3 to 4 c.c. of alcohol and overlaid on concentrated sulphuric acid, a blue zone appears at the point of contact.

A carefully prepared dialyzed extract of the fresh root in 60 per cent alcohol contains both glucosides, gentiopicrin, and gentiamarin; it is fluorescent, and from it both glucosides may be removed by ethyl acetate.

The glucoside-tannin acid compound is transferred to a beaker, alcohol added followed by zinc hydroxide, and boiled gently until the compound is broken up and the tannic acid combined with the zinc. Evaporate the alcohol at 40–50°, extract with hot absolute alcohol to remove the glucosides, filter, and evaporate the solvent at 40–50°.

Helleborein is intensely bitter, causes sneezing and dissolves in water. It dissolves in concentrated sulphuric acid to a golden-yellow solution, becoming reddish brown. On hydrolysis with dilute acid, under a reflux, it yields dextrose and helleboretin, the latter being a violet blue substance when moist.

Convallamarin gives a brown to purple color with concentrated sulphuric acid.

Digitalis glucosides dissolve in concentrated sulphuric acid to a golden-yellow solution, which on the addition of a hypobromite or exposure to bromin fumes changes to a rose red or violet color. If dissolved in glacial acetic acid containing a trace of ferric chloride and carefully overlaid on sulphuric acid a deep carmine red zone appears.

Adonidin is precipitated by tannic acid, but not by lead salts.

Saponins.—Tests for these substances can be made with a portion of this liquid or of the original solution. The solution should first be treated with magnesium hydroxide to remove tannins and then with barium

chloride in slight excess, filtered and the filtrate precipitated by lead subacetate. The lead precipitate is separated by centrifuging, decomposed by hydrogen sulphide in the presence of water, the solution filtered, neutralized with calcium carbonate, concentrated, extracted with ether, which is discarded, the residue dissolved in water, filtered, and evaporated to a syrupy consistency and then dropped into an excess of absolute alcohol, which will cause a precipitation of the saponin.

Another procedure is as follows: After removing the tannin with magnesium hydroxide, neutralize with magnesium carbonate, add 20 grams ammonium sulphate and 10 c.c. phenol; after shaking, the phenol solution is separated and shaken with 50 c.c. water and 100 c.c. ether, with the addition of alcohol if necessary to prevent emulsification; the aqueous layer is drawn off and allowed to dry in a desiccator, and the residue washed with acetone or ether.

If dextrin is present, the liquid should be concentrated to 20 c.c. and precipitated with 100 c.c. of 95 per cent alcohol; after standing thirty minutes, the mixture is boiled on the water-bath, filtered, the alcohol removed by distillation, the solution diluted to 100 c.c., and then treated as above.

The saponin residue should then be dissolved in water and three portions of 3 to 4 c.c. each evaporated in porcelain dishes, and tested with nitric acid, sulphuric acid, and Froehde's reagent. Sulphuric acid develops a red to violet color with some saponins, especially on warming, and the solution may become fluorescent. Froehde's reagent produces a purple shade.

Quillaic acid gives a dark-red color with concentrated

sulphuric acid and quillaja saponin, a yellowish color changing slowly to reddish. These two saponins are soluble in water and the former is precipitated by normal lead acetate while the latter is not.

Polygalic acid from senega gives a ruby-red color with concentrated nitric acid changing to yellow and yellowish red. It gives a red to violet with concentrated sulphuric acid. Senegin gives a yellow color with nitric acid.

To portions of the aqueous solution add gold chloride, mercuric chloride, ammoniacal silver oxide, potassium ferricyanide and permanganate which will be reduced. An alkaline copper solution will give a green gelatinous precipitate, soluble in water.

A hemolytic test may be performed if desired, with a suspension of red blood corpuscles prepared by washing sterile, defibrinated animal blood by centrifuging three times with physiological salt solution and when the solution is clear removing 5 c.c. of the red corpuscles and diluting with 100 c.c. of the salt solution. A portion of the latter, well mixed, is treated with the saponin solution which will cause hemolysis, recognized by the reddening of the solution, and at the same time the cloudy suspension becomes clearer. This test is not always positive because the manipulation of some of the saponins by means of lead salts appears to change their physiological action, and some saponins appear to have very little action on the blood.

Hexamethyleneamine.—If this body is indicated, acidify a portion of the solution with hydrochloric acid, add a slight excess of iodin solution, filter, wash precipitate three times with water, then transfer to beaker, using a stream of water to wash it off the paper. Add a few crystals of

sodium sulphite, stirring until the precipitate is dissolved and the liquid colorless, add a few c.c. of dilute sulphuric acid and boil gently. Note odor of vapor for formaldehyde; withdraw flame, invert over the fumes a porcelain dish smeared with sulphuric acid containing morphin and after exposure for several minutes, note the color of the acid, which should be deep purple if formaldehyde is present. Continue boiling the liquid in presence of acid until concentrated, cool dilute with 10 per cent sodium hydroxide, warm and note the evolution of ammonia vapor, recognizable by its characteristic odor and action on litmus paper and phenolphthalein paper.

Phenolsulphonic Acids.—Paraphenolsulphonic acid or its salts on treatment with bromin water yield a precipitate of tribromphenol and the sulphonic group is oxidized to sulphuric acid. The solution is acidulated with hydrochloric acid, heated just short of boiling and barium chloride added to precipitate any sulphates which may already be present. Filter, wash precipitate, add bromin water to filtrate which will throw out both tribromphenol and barium sulphate. Filter, transfer to a small beaker, cover with water and add acid sodium sulphite solution until a strong odor of sulphur dioxide remains after stirring and warming to 40°. Filter, wash with cold water, treat with boiling 40 per cent alcohol, which will dissolve the tribromphenol, and which will be deposited from the filtrate on cooling. Filter, dry on porous plate. The melting-point should then be observed, which is 92.5–93.5°.

Aloin.—Acidulate a portion of the solution with acetic acid and add bromin water drop by drop, at half minute intervals. A dun-colored precipitate comes down at

first and a gradually appearing violet-red color develops in the solution, then as an excess is added a yellow shade appears and the precipitate on filtering is found to be bright yellow. The precipitate should be washed and recrystallized out of dilute alcohol and dried on unglazed porcelain. Tribromaloin melts 191-192°.

Treat another portion of the ammoniacal solution with calcium chloride. Aloin gives a precipitate. This test is of no value if acid radicals which form insoluble salts with calcium are present.

Further tests for aloin should be made on a fresh portion of the original alcoholic extract. Evaporate to dryness, treat with hot water, filter, evaporate to dryness, extract with absolute ether or chloroform, then treat with hot absolute alcohol and filter. Evaporate a few drops of the alcoholic solution in a porcelain dish and add nitric acid, which will give a deep red color with aloin. Evaporate another portion and add a few drops of sodium hydroxide, which will give a deep orange-red fluorescent solution. The balance of the alcohol is then evaporated and the residue dissolved in hot water. The solution should be tested with bromin water as above described and portions tested as follows: A drop of ferric chloride produces a reddish-violet color changing to greenish black as more of the reagent is added. Calcium chloride gives a precipitate from a solution made slightly alkaline with ammonia.

A residue of nataloin when dissolved in concentrated sulphuric acid gives a blue color when exposed to the vapor of nitric acid.

Glycerin.—Ten to fifteen c.c. of the solution are evaporated with 5 to 10 grams of clean uniform sea sand and

5 to 10 c.c. milk of lime (containing 15 per cent CaO) to a pasty consistency. Add 50 c.c. alcohol 90 per cent, remove the substances adhering to the sides of the dish and rub the whole mass to a paste. Heat on steam-bath to incipient boiling, stirring constantly and decant liquid through a filter paper into an evaporating dish. Wash the residue by decantation with 10 c.c. portions of hot 90 per cent alcohol, until the filtrate measures 150 c.c. Evaporate the filtrate to a syrupy consistency at a temperature below the boiling-point of water, transfer the residue to a small graduated cylinder with 20 c.c. absolute alcohol, and add three parts of 10 c.c. each of anhydrous ether, shaking after each addition. Let stand until clear, then pour off through a dry filter, wash cylinder and filter with a mixture of 1 part absolute alcohol and $1\frac{1}{2}$ parts anhydrous ether. Evaporate to a syrupy consistency, dissolve in water and if colored, add a small portion of bone charcoal, heat to boiling and filter.

Divide the filtrate into two portions. To one portion add about 200 c.c. water, 10 grams potassium hydroxide and an excess of potassium permanganate (an excess is present when the liquid is no longer green, but shows a bluish or magenta color). Boil gently for an hour, then add drop by drop a saturated solution of sodium sulphite until the solution is just decolorized. Allow precipitate to settle, decant liquid through a filter, make acid with acetic acid, add an excess of calcium chloride and allow to stand in a warm place for three hours. A white precipitate of calcium oxalate will come down if glycerin was present. It should be filtered off, washed with hot water, transferred to a flask, 10 c.c. concentrated sulphuric acid added and N/10 permanganate

added, until a pink color is obtained. The white precipitate may contain sulphates, silicates, and other impurities, but the decolorization of permanganate will indicate oxalate.

The other portion of the filtrate is then evaporated and subjected to the following tests:

Mulliken's Test.—The residue is diluted with water to about 1 per cent treated with 5 drops of 1 per cent solution pyrogallic acid and 3 c.c. sulphuric acid, and boiled for about half a minute, when in the presence of glycerin a purple color begins to develop. On cooling and adding 20 c.c. alcohol, the color shows to advantage.

To perform Denigè's test for glycerin, about 0.2 gram of the residue is heated for twenty minutes on a water-bath with 10 c.c. bromin water, and then boiled until the bromin is expelled. 0.2 c.c. of this solution is treated with 0.1 c.c. alcoholic 5 per cent solution of codein, 2 c.c. water, and 2 c.c. sulphuric acid, and heated in a water-bath, when a greenish-blue color will be observed. 0.4 c.c. portions of the same solution are treated, respectively with 0.1 c.c. alcoholic solutions of resorcinol thymol, 5 per cent each, and beta naphthol 2 per cent and 2 c.c. sulphuric acid; in the cold the resorcinol gives a blood-red color, and the thymol a wine-red color, changing to rose on dilution; with the beta naphtol an emerald green with a greenish fluorescence appears on warming.

The aqueous solution A (page 5) which was originally set aside should now be examined for formates, acetates, valerates, sulphides, sulphites, thiosulphates, phosphates, hypophosphites, glycerophosphates, citrates, tartrates and lactates and ammonium salts, using about one-half of the volume. Then evaporate the balance, ignite

cautiously, treat residue first with water, then with hydrochloric acid if anything remains undissolved in water, and examine for metals and acid radicles by the procedure outlined on pages 109 to 117.

To test for formic, acetic and valerianic acid, transfer a portion to a distilling flask fitted for steam distillation, add a small quantity of phosphoric acid, and conduct distillation. If distillate is acid in reaction note odor, which will be that characteristic of valerianic acid if this substance is present. Add barium carbonate to distillate and evaporate to dryness. Treat with a small quantity of water, warm, filter. Divide the filtrate into several fractions.

To one portion add ammoniacal silver oxide and a white precipitate soon turning dark indicates a formate. To another portion add 1 c.c. sodium acetate, 2 c.c. dilute hydrochloric acid and 2 c.c. mercuric chloride and a white precipitate of calomel occurs in presence of a formate.

Treat a portion with a few drops of ferric chloride, which will give a deep-red color if an acetate is present; on warming a heavy deposit of basic ferric acetate results. To another portion add an equal volume of ethyl alcohol, followed by 3 to 4 drops of concentrated sulphuric acid and warm; ethyl acetate will be evolved. Formic acid gives a red color with ferric chloride.

Tests for Sulphur Acids.—Agitate with lead carbonate, which will turn black if a sulphide is present. Filter. Treat filtrate with barium chloride in slight excess, allow precipitate to settle and filter and wash precipitate. To filtrate add hydrochloric acid, which will cause a precipitation of sulphur and liberation of sulphur dioxide if a

thiosulphate is present. The barium precipitate is then treated with hydrochloric acid, which will dissolve the sulphite, and on filtering and adding chlorin water to the filtrate the sulphurous acid will be oxidized to sulphuric acid with precipitation of barium sulphate.

Phosphates, Hypophosphites, and Glycerophosphates.—Make alkaline with sodium carbonate and boil off ammonia. Add barium chloride, which will precipitate phosphates. Filter, dissolve precipitate in nitric acid, add ammonium molybdate, and warm, noting precipitate. To filtrate from barium precipitation, add slight excess of sulphuric acid and silver nitrate and if a precipitate forms turning rapidly brown and black, hypophosphites are indicated. Filter, evaporate filtrate and boil with a mixture of sulphuric and nitric acids until colorless. Dilute, add ammonia, then nitric acid and ammonium molybdate and if a yellow precipitate comes out glycerophosphates are indicated.

Lactic acid when subjected to distillation with steam in presence of sulphuric acid and bichromate will evolve formic acid and acetaldehyde. The distillate will give the reaction for formic acid and redden decolorized fuchsin.

Tartaric and Citric Acids.—Treat the solution with excess of lead acetate. Filter and wash first with water and then with 50 per cent alcohol until free from lead. Wash the precipitate into a flask and decompose with hydrogen sulphide in the presence of dilute ammonia. Filter from the lead sulphide, boil to expel ammonia and ammonium sulphide, and filter again if necessary. To a portion of the filtrate add ammoniacal silver oxide and warm, noting the production of a silver mirror if tartaric

acid is present. To another portion (cool) add calcium chloride and allow the precipitate time to settle out, filter, heat filtrate to boiling and a heavy white precipitate will come out, dissolving again on cooling if citric acid is present.

Ammonium Salts.—To test for ammonium salts, treat a portion of the solution with strong sodium hydroxide in a small beaker, cover with a watch-glass to the under surface of which is a moist strip of red litmus paper and place on steam-bath. Ammonia will be evolved in this test, recognizable by the rapid change in color of the litmus and the characteristic odor of the vapor. Usually on subjecting a piece of red litmus paper to the vapors evolved from an organic mixture which has been treated with alkali, a blue color will gradually develop if the mixture is allowed to stand over the steam-bath for ten to fifteen minutes. The reaction, however, is not due to ammonium salts.

2. Substances Soluble in Alcohol, but Insoluble in Water

Consult list on page 8.

Note the appearance of the residue. Iodoform, salol, camphor monobromate, asafetida, copaiba, aromatic balsams and turpentine have characteristic odors and are easily recognized.

If resins are present dissolve a portion in alcohol, the quantity to be employed depending somewhat on the amount of material. Divide into four portions. If phosphorus is suspected divide into five fractions and test one portion as described on page 2.

To one portion add an equal volume of petroleum ether and shake, then add water and shake for thirty seconds. Separate and draw off aqueous layer, and wash petroleum ether with water until both layers are clear. Add a 0.5 per cent copper acetate solution and shake. The appearance of a green color in the petroleum ether indicates abietic acid (from colophony).

Another portion is treated with 10 c.c. strong hydrochloric acid and boiled for five to ten minutes. Cool and add excess of ammonia and note any blue fluorescence due to umbelliferone (Galbanum, African Ammoniacum, Sumbul resin).

Moisten strips of clean white filter paper with the alcoholic solution. When nearly dry expose strips to fumes of nitric acid and chlorin, and moisten another strip with tincture of ferric chloride which will develop blue shades if guaiac is present. Add a few drops to mucilage of acacia, which will gradually develop a blue tint. Mammalian blood stains moistened with the alcoholic solution and followed by a few drops of dilute hydrogen peroxide become blue.

Treat another portion with sodium hypochlorite, which will produce a violet color in presence of Ammoniacum.

Now treat the balance of the residue with ether, filter into a separator and shake out with normal sulphuric acid; separate the acid, add ammonia, shake out with ether, filter, evaporate solvent and examine the residue for alkaloids.

Then shake out ether solution with sodium bicarbonate, separate, add hydrochloric acid in excess, shake with ether, wash ether layer with water, filter, and evaporate.

The residue may contain benzoic, cinnamic, salicylic, ferulic, cumaric, and other acids.

Shake out ether solution with dilute sodium hydroxide and note color, which may be pink or reddish, due to anthraquinone constituents of chrysarobin, aloes, or other anthraquinone drugs and phenolphthalein. Separate alkaline layer and continue extraction until no further color is removed. Combine alkaline solutions, add excess of hydrochloric acid, and shake out with ether. Wash ether, filter, and evaporate. According to the color indications examine residue for phenolphthalein, anthraquinone derivatives, also naphthols, guaiacol from Guaiac, following the suggestions on pages 27 and 31.

The ether solution which had been shaken with sodium hydroxide is then washed with water which is discarded and the ether evaporated. Test residue for santonin. The residue is then treated with alcoholic potash or soda and boiled under a reflux for an hour. The solution is measured, transferred to a separator, an equal volume of petroleum ether added, followed by the same volume of water and the solution allowed to separate. Wash the petroleum ether with water, reserving petroleum ether solution designated (*A*), add the washings to the alcohol-water layer and evaporate off the alcohol. Transfer to separator, washing out with water, add sulphuric acid in excess and shake out with ether. Separate ether and reserve acid liquid (*B*). Shake ether with sodium bicarbonate, separate, acidulate, shake out with ether, separate, wash ether, filter and evaporate, examining residue for acid products which may have been set free on saponification. The ether layer which had been shaken with sodium bicarbonate is now shaken

with dilute sodium hydroxide and the alkaline liquid separated, acidulated, shaken with ether and the solvent evaporated, testing the residue for thymol if thymol diiodide had been indicated, and carbolic acid if salol had been suspected. The ether layer which had been shaken with alkali is then washed with water and evaporated spontaneously and examined for camphor and cantharidin.

The acid liquid (*B*) above is then tested for halogens freed from iodoform, thymol diiodide, camphor monobromate, etc., by saponification.

Evaporate the petroleum ether solution (*A*) and examine for camphor, turpentine, Canada balsam, copaiba, and other resinous constituents.

There is summarized below the chief characteristics of the more common resins found in medicinal preparations. The acids united to the tannols will be liberated at least partially by the saponification procedure, and their identification by following the above scheme will aid in recognizing the resins.

Aloe Resin.—Barbadoes aloes contains a cinnamic acid ester of aloeresinotannol.

Cape Aloes contains the *p*-cumaric acid ester of aloeresinotannol.

Natal Aloes Resin contains the *p*-cumaric acid ester of nataloresinotannol. On saponification, the resinotannol is obtained as an aromatic powder soluble in alkalies, and the characteristic acids can be separated by acidifying the alkaline liquid and shaking out with ether.

Ammoniac contains about 60 per cent of resin solubl in ether. It contains ammoresinotannol united to

salicylic acid, which may be obtained on saponification. Ammonia also contains a portion of gum. Umbelliferone is absent.

African ammoniac contains umbelliferone.

Asafetida has a characteristic odor, and consists of about 62 per cent of the ferulic acid ester of asaresinotannol, free asaresinotannol, ethereal oil, ferulic acid, and a trace of vanillin. Ferulic acid on fusion with alkali yields resorcin and protocatechuic acid.

Benzoin.—Siam benzoin contains only benzoic acid. Sumatra benzoin contains cinnamic and benzoic acids. Singapore benzoin contains cinnamic and benzoic acid. Sumatra benzoin contains vanillin, cinnamic acid-phenylpropylester and styracin, cinnamic acid united with resinotannol, and a little benzoresinol. Siam benzoin contains the benzoic ester of benzoresinol and siaresinotannol.

Bryony resin is dark brown and viscid, and contains bryonol, a dihydric alcohol, melting 210–212°, and yielding a diacetyl derivative melting 152°. Bryonol in acetic anhyride gives with sulphuric acid a purplish-pink color changing to blue, green, and brown.

Canada balsam contains a levoterpene, $C_{10}H_{16}$, boiling at 167°, and giving with hydrochloric acid a crystalline compound; canadinic acid soluble in ammonium carbonate, canadolic acid, alpha- and beta-canadinolic acids, ethereal oil and canadoresene. Alpha-canadinolic acid is soluble in ordinary solvents, gives the cholesterin reaction, and is precipitated by alcoholic lead acetate. Beta-canadinolic acid is not precipitated by alcoholic lead acetate. The balsam solidifies when mixed with magnesium oxide and water.

Cannabis resin is dark green. Extract the resin with low-boiling petroleum ether, filter and evaporate. Treat the residue with absolute alcohol which has been saturated with dry hydrochloric acid gas when a bright cherry-red color will develop. On adding water or alcohol the color disappears.

If a capsule containing the resin is introduced into the stomach of a small dog by placing it on the back of the tongue, closing the mouth and gently slapping the throat until swallowed, characteristic physiological effects will soon develop, the animal at first becoming restless, then losing coordination and finally losing all control of the muscles of the limbs and neck and falling into a stupor and sleep.

Copaiba consists of volatile oil, amorphous and crystalline resin acids and resenes. The characteristic odor due to the volatile oil is sufficient evidence of its identity.

Damiana.—The resin is dark green in color, and has a characteristic odor.

Fabiana imbricata (*pichi*).—The resin contains fabianeresene, which is soluble in ether and sublimes. On treatment with sulphuric acid it turns yellow, and the solution becomes red on warming. On adding water to this solution a colorless amorphous precipitate is obtained. Its solution in phenol is colored yellow-brown on heating with zinc chloride, and on adding sulphuric acid a rose-red color appears, soon changing to purple.

Galbanum contains a volatile oil, resin and gum. The resin is soluble in ether and alkalies, contains free umbelliferone and umbelliferone combined with galbanoresinotannol.

Gamboge consists of resin, gambogic acid, and gum.

It has a characteristic yellow color. It is soluble in alkalies.

Grindelia resin is dark green and has a characteristic odor. A soft sticky fraction dissolves in petroleum ether and the balance of the resin is almost entirely taken up by ether.

Guaiac consists of resin, resin acids, guaiacol and a yellow coloring matter.

Gurgun Balsam.—This balsam has an odor like copaiba. When a few drops are dissolved in glacial acetic acid, treated with 1 drop of freshly prepared sodium nitrite 1 : 10 and underlaid with concentrated sulphuric acid, the acetic acid layer will develop a pink tint.

Hop Resin.—Ether solution after first washing with ammonium carbonate solution, will yield humulol to sodium carbonate and then xanthohumulol to sodium hydroxide. On acidifying the alkaline liquids and shaking out with ether the substances can be recovered. They are phenolic bodies giving intense yellow alkaline solutions, but no color with ferric chloride.

Jalap resin is only partially soluble in ether while Scammony is almost completely soluble. To test for jalap treat the resinous matter with ether and filter from the undissolved residue. Warm the residue until ether is driven off and then treat a portion with concentrated sulphuric acid, which will produce a brown to blood-red color with a noticeable jalap-like odor. The balance of the residue is treated with chloroform and filtered, the chloroform solution shaken with sodium carbonate, which will show a blue fluorescence due to methylaesculetin.

Leptandra resin amounts to 6 to 7 per cent of the drug

yielding a phytosterol melting 135–136°, acetyl derivative melting 119–120°, and on hydrolysis oleic, linolic, palmitic, stearic, paramethoxycinnamic, and 3.4-dimethoxycinnamic acids.

Herabol myrrh contains 50 to 75 per cent gum, 25 per cent resin containing two resin acids and 2.5–8 per cent volatile oil. On treating 6 drops of a solution of bisabol myrrh in petroleum ether with 3 c.c. glacial acetic acid and 3 c.c. concentrated sulphuric acid, a rose-red zone appears which is quickly communicated to the acetic acid portion; with herabol myrrh the acetic layer develops a very pale rose color which does not increase in depth, and the surface of contact between the two layers shows at first a green color, which turns brown with a green fluorescence on standing.

Olibanum contains 72 per cent resin soluble in alcohol, and 28 per cent insoluble. The former contains a large quantity of boswellinic acid, a small amount of the acid combined as ester, olibanoresene, terpenes, and a bitter substance; the latter contains gum, bassorin, and plant residue. Olibanoresene is soluble in organic solvents and insoluble in alkalies. Boswellinic acid has a melting-point of 150°. It forms a blue salt with copper.

Opopanax (umbelliferous) consists of ether-soluble resin (ferulic acid ester of oporesinotannol), a small amount of ether insoluble resin, gum, ethereal oil, and small quantities of ferulic acid. Burseraceous opopanax contains a smaller amount of resin and a larger quantity of gum than the other variety. Its odor resembles Sumbul and Bisabol myrrh, and it is commonly designated as Myrrh in the East.

Peru balsam has a molasses-like consistency and con-

sists largely of benzyl benzoate, a colorless oil, free vanillin, free cinnamic acid, and a resin consisting of the benzoic- and cinnamic-acid esters of peruresinotannol. Cinnamein or Peru balsam oil, the oily liquid separating on agitation with alkali, contains benzyl benzoate, benzyl cinnamate, benzyl alcohol, and other aromatic compounds.

Podophyllum.—The resin contains podophyllotoxin and picropodophyllin. The resin is intensely irritant to the mucous membrane of the eye and if dried and powdered will usually produce conjunctivitis.

Sandarac contains the hydrocarbon *d*-pinene, and a diterpene and *i*-pimaric and callitrolic acids.

Asiatic scammony (Convolvulus scammonia) resin has saponification value 179–229, acid number 14–28. Mexican scammony (Ipomoea orizabensis) resin has saponification value 180–185, acid number 14–15. Taylor shows that pure scammony resin from both sources is soluble in ether, 96–97 per cent true resin, having saponification value above 230, while that of the Mexican is between 185 and 200.

The solubility of the resin in ether distinguishes scammony resin very sharply from Jalap. To test for scammony extract the residue with ether, filter and evaporate. Expel the ether and rub a portion of the residue in a mortar when the characteristic odor of scammony will be developed. Another portion is warmed with sodium carbonate solution until nothing further dissolves; the insoluble portion, after washing with water and dried, on adding concentrated nitric acid, will swell up to a yellow mass.

Storax is a viscid, grayish, somewhat opaque mass,

containing cinnamic acid, styrol, styracin (cinnamyl or styrylcinnamate), cinnamic acid-ethyl ester, cinnamic acid-phenylpropyl ester, and storesinol; the latter is soluble in alkalies and on distillation gives phenol, cresol, benzol, and toluol; on oxidation with permanganate it yields phthalic acid, benzoic acid, and an acid insoluble in water.

Tolu balsam when fresh has a soft tenacious consistency but not viscid like Peru. On aging it becomes hard and brittle. It consists largely of a resin which is a combination of tolu resinotannol with cinnamic acid, and a small amount of benzoic acid. It also contains an acid aromatic oily liquid, chiefly benzyl benzoate, with a little benzyl cinnamate, about 20 per cent of free cinnamic acid, and small quantities of a volatile oil and vanillin.

3. Substances Insoluble in Alcohol, but Soluble in Water.[1]

This fraction will contain sucrose if it was present in any quantity, and many salts of organic and inorganic acids. A portion should first be tested for acids which are altered by heat as described on page 90, looking especially for glycerophosphates, special tests performed for the few organic bodies liable to be present, and then the balance ignited cautiously, and the residue tested for metals and acids. See pages 109 and 117.

Proteins.—Five c.c. of the solution to be tested are mixed with a few drops of formaldehyde, a trace of dilute ferric chloride added, and the mixture overlaid on sul-

[1] Fraction b, page 5.

phuric acid in a test-tube; if proteins are present a violet ring appears at the junction.

If 1 to 2 c.c. of the solution are treated with 2 to 4 drops of a 5 per cent solution of sodium nitroprusside, and then a few drops of ammonia, a purple-red color appears, destroyed by acetic acid.

A similar reaction may be obtained with a precipitate obtained by means of ammonium, magnesium, or sodium sulphate, phosphotungstic acid, or alcohol. The precipitate is washed, placed on a piece of porous paper, moistened with a few drops of nitroprusside and ammonia added, whereupon a purple-red color appears.

If 5 c.c. of the solution are treated with Millon's reagent and boiled, a white precipitate is obtained which turns brick-red on boiling, and the supernatant liquid becomes red on standing.

Five c.c. of the solution are treated with a few drops of a very dilute solution of copper sulphate followed by a slight excess of sodium hydroxide. In the presence of certain proteins a blue precipitate will be thrown out by the copper which will dissolve in the alkali with the production of a violet color.

Carbohydrates.—To 5 c.c. of a dilute solution of the residue add a few drops of 15 per cent solution of alpha naphthol; float this over concentrated sulphuric acid and a violet or blue zone at the line of contact indicates a carbohydrate.

To a fairly strong solution of the residue add an equal volume of 95 per cent alcohol. A precipitate indicates dextrin and also inulin, acacia, and other constituents of gum soluble in water. Filter and wash with 50 per cent alcohol. Dissolve in water and add iodin solution,

which will give a reddish-brown color if dextrin is present. Inulin gives a yellowish color with iodin. Neither dextrin nor inulin reduce Fehling's solution. If acacia is suspected, treat an aqueous solution of the precipitated substance with a few drops of tincture of guaiac, which will produce a blue color, gradually appearing.

To a fairly strong solution of the residue add Burford's solution of copper acetate and boil; reduction indicates dextrose or levulose or both. Filter. Add basic lead acetate, warm and allow to stand until precipitate settles, filter, precipitate excess of lead with sodium sulphate, filter (if solution is not blue add a few drops of copper sulphate), make alkaline with sodium hydroxide and boil; reduction indicates maltose or lactose or both. Filter. To filtrate add sulphuric acid in slight excess and boil for a few minutes, add an excess of sodium hydroxide and a few drops of copper sulphate and boil; reduction indicates sucrose.

To another portion of an aqueous solution of the residue add excess of ammonia and a few drops of alkaline bismuth solution. Set tube in water-bath at 60°. Reduction takes place almost immediately in presence of maltose, while lactose does not reduce bismuth at this temperature for one-half hour.

To detect lactose add a portion of the residue to 5 c.c. concentrated nitric acid and warm gently until red fumes are evolved. Set tube in hot water and allow it to remain there until cold. In a few hours white crystalline mucic acid separates if lactose is present.

Mannitol, a sweet-tasting alcohol from manna, insoluble in ether and without action on Fehling's solution will, occur in this fraction.

4. Substances Insoluble in Alcohol and Water.[1]

In this fraction we will meet with starch, calcium carbonate, and siliceous material, and other substances used as diluents in the making of pills and tablets. There will be present but few organic active principles except possibly some cantharidin, and a few of the compounds of organic substances and bases which can be determined from the table. Starch is readily detected by treating a bit of the residue with iodin solution. Bismuth subgallate is soluble in alkali to a yellow solution, and giving a black sulphide on treatment with hydrogen sulphide, in which the metal can be identified by separating and making appropriate tests. The citrate will also dissolve in alkali.

The residue should then be treated successively with hydrochloric acid, nitric acid, and aqua regia, and each solution examined according to the regular procedure for basic and acid analysis. In drug products the active ingredients will hardly be other than those given in the tables.

Arsenic.—All medicinal preparations should be examined for arsenic, the tests being carried out on a fresh sample, and not on the solution employed in the previously described separations. The product should be digested first with nitric acid, then evaporated, treated with sulphuric acid, heated until well charred, more nitric acid added, again heated, and this procedure repeated until the final solution is nearly colorless and all nitrous fumes are driven off. This solution may then

[1] Fraction 4, page 10.

be introduced directly into the Marsh apparatus or subjected to any reliable test approved by the analyst.

Scheme of Analysis for Identifying the Metals and Acid Radicals

The test for the inorganic components of a medicinal compound are made with the solutions *A* and *b* and residue 4 noted on pages 5-6-10.

Note the preliminary tests on *A* noted on page 90.

For a detailed account of what to do and how to proceed with the complete qualitative analysis of a complex mixture the worker can refer with advantage to my directions for manipulating an elixir.

Preliminary Observations on Recognizing Inorganic Constituents

The principal inorganic substances or salts of inorganic bases with organic acids used in medicine which are insoluble in water, are iodin, mercuric iodide, phosphorus, sublimed sulphur, iron valerinate, bismuth subnitrate, subcarbonate, citrate and subgallate, cerium oxalate, calcium fluoride, reduced iron, charcoal, red and yellow mercuric oxide, mercurous iodide, mercurous chloride, precipitated sulphur, zinc carbonate, oxide and phosphide, magnesium oxide and carbonate, and a few organic compounds of bismuth, aluminum, calcium, and iron. The first three mentioned are of course soluble in alcohol.

In addition to these a medicinal compound may contain calcium carbonate, sulphate or phosphate, ignited oxides of iron and aluminum, talc, clay, and siliceous

compounds, and possibly other heavy inert salts which take part in the architecture of the sample.

Of the above substances, all are soluble in hydrochloric acid except iodin, phosphorus, sulphur, charcoal, calcium fluoride, mercurous iodide, mercurous chloride, ignited oxides of iron and aluminum, talc, and clay. Mercuric iodide does not dissolve in dilute hydrochloric acid but it goes into solution with the warm concentrated acid. Mercurous chloride is converted into mercuric chloride by aqua regia, mercurous iodide is dissolved, sulphur, and phosphorus partly oxidized and some of the oxides of iron and aluminum dissolved. The organic compounds will be decomposed to a greater or less degree by boiling with the acids and the metals will be found in both the hydrochloric and aqua regia fractions.

The analyst should note carefully any gases evolved, when the unknown product is treated with hydrochloric acid. The carbonates will of course give off carbon dioxide, and if zinc phosphide is present, hydrogen phosphide with its characteristic odor and inflammability, will be apparent.

The commoner substances other than those we have already mentioned, which are insoluble in water and acids, are the sulphates of barium, strontium, and lead, the silver haloids, silver and iron cyanides and tin oxide. Their presence in medicinal products would be most unusual.

In examining the residue insoluble in acids, the presence of free sulphur and charcoal is noted without difficulty. Iodin, unless in large amount, will probably have been dissipated by boiling and recognized by the purple vapors evolved. At this point in the well-

ordered schemes a test is made for lead and silver. The former is found by treating the residue with ammonium acetate solution, warming, filtering, and testing the filtrate with hydrogen sulphide. If lead is present, as shown by a black precipitate, the residue, both in the dish and on the filter, must be washed with warm ammonium acetate until there is no reaction for lead. The insoluble portion is then tested for silver by warming with potassium cyanide solution, filtering and testing the filtrate with hydrogen sulphide. If silver is found it must be removed by successive treatments with the cyanide reagent. The residue is then washed clean with yellow ammonium sulphide, the filtrate tested for tin and the insoluble matter on the filter washed with water.

Sulphur and carbon should then be burned off in a porcelain crucible and the residue fused in a platinum crucible with a fusion mixture of sodium carbonate 2, potassium carbonate 2, and potassium nitrate 1. After a state of quiet fusion has been attained and the mass cooled, it is leached out with hot water and in this solution will be found the acids present in the original residue, united to the bases of the flux. Aluminum and chromium might also be present in the aqueous solution in the form of aluminate and chromate. The metals present will go into an hydrochloric acid fraction.

The aqueous solution should be acidified with hydrochloric acid and evaporated nearly to dryness in order to convert any silicic acid to insoluble silica. A solution obtained by leaching out any silica residue can then be tested for sulphates, fluorides, aluminates and chromates. The hydrochloric acid fraction may contain barium, strontium, calcium, iron, aluminum, and chromium.

Scheme of Analysis for Identifying the Metals

After obtaining an aqueous solution its reaction to litmus should be noted and a sufficient quantity set aside for testing for acid radicles.

Now treat one of the subdivisions in the cold with a little dilute hydrochloric acid, noting any effervescence due to the evolution of *carbon dioxide* or *hydrogen phosphide* and test the gases with a lighted match. Carbon dioxide will extinguish the flame and hydrogen phosphide will ignite and deposit phosphorus pentoxide on the walls of the tube as it burns. Also test with lead acetate paper and note odor in case sulphides are present, and note whether sulphur dioxide is evolved indicating sulphites and whether there is a simultaneous precipitation of sulphur due to thiosulphates. The addition of dilute hydrochloric acid will also precipitate *lead*, *silver* and *mercurous mercury*. Filter and wash with cold water, setting aside filtrate. Then treat the precipitate of the insoluble chlorides with hot water, test washings with sulphuric acid and hydrogen sulphide for lead whose chloride dissolves in hot water. If lead is found, the washing with hot water must be continued until it is all removed and then the insoluble portion on the filter is treated with ammonia water. If the precipitate turns black the presence of *mercurous* mercury is established and the filtrate will contain the silver chloride which is precipitated by adding an excess of nitric acid.

Arsenic and Copper Groups.—The filtrate from the hydrochloric acid precipitation is heated nearly to boiling and subjected to a prolonged treatment with hydrogen sulphide. By this treatment lead, copper, bismuth, and

gold are immediately precipitated as black sulphides, arsenous arsenic, antimony, and stannous tin come down without delay, mercuric mercury yields a precipitate which may be yellow or red but which finally becomes black, and cadmium gives a tardily appearing yellow precipitate. The higher forms of tin and arsenic are not precipitated as rapidly as the lower. Ferric salts and chromium compounds are reduced with precipitation of sulphur. After the precipitation is complete, filter and wash with hot water, setting aside filtrate for future treatment. Solution F.

Treat precipitate with yellow ammonium sulphide and warm. Any sulphur and the sulphides of arsenic, tin, antimony and gold together with a little of the copper sulphide will dissolve, the solution containing the thio salts of these metals. Filter and reserve precipitate.

Arsenic Group.—Add hydrochloric acid drop by drop until in excess, filter, wash with water, boil with hydrochloric acid, dilute and filter. The filtrate should be concentrated and a piece of iron wire added and the evolution of hydrogen induced by the addition of a little hydrochloric acid. *Antimony* will be deposited as a black precipitate; filter, test filtrate with mercurous chloride, and white precipitate of calomel will indicate *tin.* Black precipitate, wash with water and add cold tartaric acid solution, followed by a drop of nitric acid, dilute and pass in hydrogen sulphide. Red precipitate shows antimony. The precipitate may now consist of the sulphides of *arsenic* and *gold.* Dissolve in hydrochloric acid and potassium chlorate or aqua regia, boil off excess of acid and introduce half of the solution to a Marsh generator

and test gases evolved for arsenic. The other half of the solution is then tested for gold by warming a portion with oxalic acid which will cause a deposition of the metal on the sides and bottom of the tube and another portion with stannous chloride which will give a precipitate varying from reddish brown to purple.

Copper Group.—Wash with water the sulphides which had been subjected to the treatment with yellow ammonium sulphide. Treat with boiling dilute nitric acid which will dissolve all of the sulphides except mercury. Any undissolved residue must be treated with concentrated hydrochloric acid and potassium chlorate and boiled, on diluting, the solution should be filtered, divided into two parts, one treated with clean copper wire on which *mercury* will deposit and the other with stannous chloride, which will produce a precipitate of calomel. The solution of the nitrates obtained above is then concentrated, sulphuric acid added and evaporation continued until any lead is precipitated, dilute, filter and to filtrate add ammonia water in slight excess, which will throw out bismuth hydrate and turn the solution blue if copper is present. Filter and test precipitate for *bismuth* by dissolving in concentrated hydrochloric acid, boiling off excess and pouring into a large volume of water when a white precipitate of bismuth oxychloride will appear. The filtrate from the ammonia precipitation is divided into two portions, to one is added acetic acid and potassium ferrocyanide and red color shows *copper.* If copper is present add potassium cyanide to the other portion and boil until the blue color is discharged, then pass in hydrogen sulphide and a yellow precipitate shows *cadmium.*

The solution F may now contain the metals of the iron, alkaline earth and alkali groups.

Boil to expel excess of hydrogen sulphide, add a little nitric acid and continue boiling until iron is converted to ferric state. Add ammonium chloride in considerable excess and then a slight excess of ammonia water. The precipitate obtained may consist of the hydroxides of iron, chromium, and aluminum. Magnesium will come down at this point if the amount in solution is considerable. The precipitate with ammonia may contain also the phosphates of all the remaining metals except those of the alkali group and alkaline earth borates, and the procedure to be adopted in this case will be treated in a subsequent paragraph. If no precipitate is obtained and the solution takes on a deep wine color it indicates that citric or tartaric acids are present and under these conditions the whole scheme will have to be modified. In such a contingency first make tests for the acids, then ignite at a low heat and test for the metals in the ash.

Iron, Chromium, and Aluminum.—Boil the solution which has been precipitated with ammonia, filter and wash, reserving filtrate for detection of manganese, zinc, cobalt, and nickel. Remove a small portion of the precipitate with the end of a stirring rod, dissolve in a little dilute nitric acid, add ammonium molybdate and boil. If a canary-yellow precipitate is obtained the procedure to be observed under phosphates must be followed. If phosphates are absent, transfer the precipitate to a test-tube with a little water, add sodium peroxide and boil for a minute until the temporary effervescence ceases. Filter and any *iron* will be left on the paper as hydroxide and is confirmed by dissolving in dilute hydrochloric acid

and testing with potassium ferrocyanide and potassium sulphocyanide. The filtrate will contain the chromium and aluminum. Divide into two portions, to the first add a slight excess of acetic acid, and then lead acetate and a yellow precipitate indicates *chromium;* to the second add an excess of dilute nitric acid, and then an excess of ammonia water and on warming a heavy floculent precipitate of *aluminum hydroxide* will appear.

Cobalt, Nickel, Manganese, and Zinc.—The filtrate from the ammonia precipitation of iron, chromium and aluminum is then subjected to a current of hydrogen sulphide gas until there is no further precipitation, the sulphides filtered and washed with hot water and the filtrate set aside for further testing. The mixed sulphides are then treated with hot dilute hydrochloric acid and if they dissolve easily and were not previously black in color there can be no nickel or cobalt present. If they do not dissolve completely in hot dilute hydrochloric acid add a crystal of potassium chlorate and boil. Continue the heating until the odor of chlorin has disappeared then add an excess of sodium hydroxide and boil. Cool and filter. The precipitate may consist of the hydroxides of manganese, cobalt, and nickel, and the filtrate will contain the zinc as sodium zincate. Pass hydrogen sulphide through filtrate and if a white precipitation is obtained, soluble in hydrochloric but insoluble in dilute acetic acid, *zinc* is present.

The mixed hydroxides are thoroughly washed and dissolved in a minimum amount of warm hydrochloric acid, the solution nearly neutralized with ammonia, a considerable quantity of ammonium acetate added and hydrogen sulphide passed through, which will precipitate the

cobalt and nickel. Filter, treat filtrate with sodium carbonate to precipitate manganese, filter the manganese carbonate, wash, dissolve in dilute hydrochloric acid, add excess of sodium hydroxide, and *manganese hydroxide* will be thrown down as a white flocculent precipitate which darkens rapidly on filtering. Test with bead of sodium carbonate and potassium nitrate, which gives a robin-egg blue color. Borax bead gives wine color in oxidizing flame, colorless in reducing. The black sulphides obtained above are now washed and tested with a borax bead and a blue color will indicate *cobalt.* Dissolve in a small quantity of aqua regia, boil off acid, nearly neutralize with sodium carbonate, add little by little a freshly made solution of potassium cyanide until the precipitated cyanides are just dissolved, then add sodium hydroxide in considerable excess, and strong bromin water until the color of the bromin persists. Filter. The *nickel* will be found as a black hydrated sesquioxide and the cobalt will remain in solution as sodium cobalt cyanide. The black precipitate is washed and tested with a borax bead, nickel producing in the oxidizing flame a violet color when hot and yellow when cold.

When Phosphates are Present.—The precipitate produced by ammonia in the presence of ammonium chloride is dissolved in a little warm dilute hydrochloric acid, nearly neutralized with sodium carbonate, a mixture of sodium acetate and acetic acid (solution made up with 13.6 grams sodium *acetate* and 80 c.c. water and 20 c.c. glacial acetic acid) added and the solution boiled and filtered. The precipitate will contain the phosphates of iron, chromium, and aluminum and it may be tested for

these metals precisely as directed above when they were precipitated as hydroxides.

The filtrate from the phosphates of iron, etc., is now treated with ferric chloride until a drop of the solution on a watch-glass gives a reddish-yellow precipitate with ammonia. The mixture is then gently boiled for a few minutes, whereby the ferric acetate is converted into an insoluble basic form and the mixture then filtered. The precipitate contains ferric phosphate and basic acetate and is discarded. The filtrate which may contain any of the metals, Co, Ni, Mn, Zn, Ba, Sr, Ca, Mg, Na, Li, K, is made ammoniacal and subjected to the treatment with hydrogen sulphide as described above.

Barium, Strontium, Calcium, and Magnesium.—The filtrate from the hydrogen sulphide precipitation of the cobalt and manganese series is boiled to drive off the excess of hydrogen sulphide and filtered from any precipitated sulphur. Ammonium hydroxide is added, a little ammonium chloride, and then ammonium carbonate and the mixture warmed but not boiled. The precipitated carbonates of barium, strontium, and calcium are filtered off and the filtrate set aside for the magnesium and alkali metal tests. Wash the carbonates and dissolve in a little dilute acetic acid, add potassium chromate and warm and a yellow precipitate indicates *barium.* Filter, wash, add excess of ammonium hydroxide and precipitate with ammonium carbonate. Filter, wash, and dissolve in dilute acetic acid. Divide the acid solution into two parts and to a small portion add calcium sulphate solution, when a tardy white precipitate indicates *strontium.* To the larger fraction add a strong solution of ammonium sulphate and boil for a short time

to ensure the solution of any calcium sulphate. The precipitate consists of strontium sulphate, and after filtering and washing may be confirmed by a flame test. The filtrate from the strontium sulphate is treated with ammonium oxalate and warmed, and a white precipitate shows the presence of *calcium.*

Magnesium.—The filtrate from the carbonates is tested in small portions, first with ammonium sulphate, ammonium oxalate, and if barium, strontium, and calcium are absent, another portion is treated with sodium phosphate, which will throw out a white crystalline precipitate if *magnesium* is present.

Sodium, Potassium, and Lithium.—The balance of the filtrate from the carbonates of barium, strontium, and calcium is then concentrated and tested on a platinum wire for the presence of *sodium, potassium,* and *lithium* Of course if the procedure for the removal of phosphates has been applied in the examination of any given sample, no conclusions as to the original presence of sodium can be drawn. To determine this a small quantity of a solution of the original sample is treated with ammonia and ammonium carbonate and the filtrate from this precipitation tested for the alkali metals.

Potassium will not always be found in the spectroscope, especially if the other metals are present, hence it is advisable to evaporate the solution completely to dryness and ignite at a low heat to expel the ammonium salts, then dissolve in water, add barium hydroxide and boil, filter precipitate the barium with ammonium hydroxide and ammonium carbonate, filter, evaporate filtrate and ignite again. Dissolve in a small quantity of water and divide into two portions; to one add platinic

chloride and the other acid sodium tartrate and stir the latter vigorously with a glass rod. Both reagents will give precipitates with *potassium.*

Acids—Scheme of Analysis for Identifying the Acid Radicles

In making tests for the metals the presence of sulphides, sulphates, thiosulphates, carbonates, phosphates, arsenates, arsenites, chromates, and permanganates will have been indicated.

The solution which was not used in testing for the metals is treated with strong sodium carbonate solution and boiled until any ammonia present is entirely expelled and then filtered. If blue, due to the presence of copper, this metal is precipitated by hydrogen sulphide and after filtering, the excess of sulphide is boiled off. Divide into two portions, A and B.

Preliminary Test I. Two to 3 c.c. neutralized with dilute sulphuric acid are treated with an equal volume of concentrated sulphuric acid and a pinch of manganese dioxide, warmed, and the vapors tested with potassium iodide starch paper. If no coloration appears bromide, chloride, iodide, chlorate, and nitrite are absent.

Preliminary Test II. One to 2 c.c. of N/25 mercuric chloride are precipitated by sodium hydroxide and 1 to 2 c.c. of the unknown solution added. If the oxide of mercury dissolves the presence of an arsenate, cyanide or iodide is indicated.

Preliminary Test III. For phosphites and hypophosphites 1 to 2 c.c. of solution are treated with a slight excess of sulphuric acid and silver nitrate added. If a pre-

cipitate forms, turning rapidly brown and then black, phosphites and hypophosphites are indicated.

Preliminary Test IV. For hypophosphites. One to 2 c.c. of the solution acidulated with sulphuric acid are treated with copper sulphate and gently warmed. A yellowish-brown precipitate changing to chocolate brown indicates hypophosphites.

Test V. Phosphites in presence of hypophosphites. One to 2 c.c. of the alkaline mixture are treated with barium chloride in excess, filtered and washed and the precipitate dissolved in sufficient dilute sulphuric acid to give a moderate excess. Then add silver nitrate and if a precipitate forms turning rapidly brown and black, phosphites are indicated. Barium hypophosphite is soluble in water.

Now proceed with the systematic scheme, using one of the portions, *A*, above.

Add nitric acid then silver nitrate in slight excess. Filter.

Precipitate may contain Ferrocyanide, Ferricyanide, Sulphocyanate, Cyanide, Iodide, Bromide, Chloride.

If preliminary test indicated halogens divide into two portions.

Portion 1. Digest in cold with a mixture of 3 vols. N/2 sodium chloride and 1 vol. N/5 hydrochloric acid which dissolves the first four. Filter and discard precipitate. Add ferric chloride in excess and a dark-blue precipitate shows *ferrocyanide*. Filter and test filtrate with more ferric chloride. If blood red in color *sulphocyanate* is shown; add sulphurous acid, a little more ferric chloride and warm. A dark-blue precipitate shows *ferricyanide* Filter, add excess sodium hydroxide and add a portion

to a suspension of mercurous oxide prepared as in preliminary test II. If it dissolves in part and the undissolved portion turns gray, *cyanide* is present.

Portion 2. Treat with zinc and dilute sulphuric acid until precipitate is black. Filter. Neutralize with sodium carbonate. Filter, discard precipitate and to filtrate add N/10 potassium iodate. If sulphocyanate is present proceed as follows. To a small portion add sodium acetate and acetic acid and *iodin* will be liberated, shake with chloroform to get characteristic color. Then acidify the balance with acetic acid and boil until colorless, add potassium iodate and if color appears boil until colorless, repeating until no further coloration occurs. Then add to solution nearly one-half its volume of dilute nitric acid. Coloration due to liberated *bromin* may be confirmed by shaking out with chloroform. Then boil the main portion until colorless. Add an equal volume of concentrated nitric acid and a white precipitate insoluble on warming shows *chlorin.*

If sulphocyanate is absent, acidify the solution after addition of potassium iodate with acetic acid and proceed as above.

Filtrate from silver nitrate precipitation.

Chlorate, Arsenite, Sulphate, Sulphite, Chromate, Arsenate, Phosphate, Borate, Sulphide, Nitrite, Nitrate, Silicate, Phosphites, Hypophosphites.

Chlorate.—If preliminary test I shows absence of halogens, no chlorate is present, but if suspected, remove a small portion of solution, add a little zinc and warm. A white precipitate of silver chloride indicates *chlorate.*

Treat the balance of the filtrate with sodium chloride

in excess, filter from silver chloride. Filtrate contains the acids.

Arsenite.—To a small portion of the filtrate add sodium carbonate to alkalinity and then an excess of barium chloride. Boil and filter. Treat filtrate with hydrogen sulphide and a yellow precipitate shows presence of *arsenite.*

Sulphate.—To the major portion of the filtrate add more nitric acid and a few drops barium chloride. A white precipitate indicates *sulphate.* If present add a slight excess of barium chloride and filter.

Filtrate contains Sulphite, Oxalate, Chromate, Arsenate, Borate, Phosphate, etc.

Sulphite.—If sulphite has been indicated by odor of sulphur dioxide on acidulating before precipitating with silver nitrate in the beginning, add more barium chloride and boil. This oxidizes *sulphite* to sulphate and a white precipitate comes down. Continue boiling until precipitation is complete. Filter. Arsenites will of course be oxidized to arsenates by this treatment. Hence unless the absence of an arsenite has been proved, a test for arsenate later does not prove the presence of that ion originally. In a similar manner phosphites and hypophosphites are oxidized to phosphates.

Oxalate and Chromate.—Add more barium chloride to the filtrate from the oxidation of the sulphite. Neutralize with sodium carbonate and add a slight excess of acetic acid. A yellow precipitate indicates *chromate* and a white precipitate *oxalate.* (Chromate cannot be present if solution was colorless or if chromium was not found in making the tests for bases and aside for a limited application of chromic oxide, the compounds of chro-

mium are not used medicinally.) Filter and to the filtrate add calcium chloride and concentrate to half its volume or less. A fine white precipitate confirms oxalate. Filter. Filtrate contains arsenate, phosphate, borate, etc. Add solid ammonium chloride and agitate until dissolved, make alkaline with ammonia and add more calcium chloride. A white precipitate indicates *arsenate* or *phosphate* or both.

Filter.

Precipitate. (Tests may be omitted if no arsenic was found in testing for metals and if preliminary tests showed absence of phosphate.)

Arsenate.—Dissolve precipitate in dilute hydrochloric acid, add sulphur dioxide and boil, after excess of sulphur dioxide has been expelled, add concentrated hydrochloric acid and saturate with hydrogen sulphide. A yellow precipitate indicates *arsenate* unless arsenite has been found. If arsenite has been found a special test must be made later in portion *B* above.

Phosphate.—Completely remove arsenic by hydrogen sulphide, filter, and boil off excess. Add a little of the solution to a solution of ammonium molybdate strongly acidulated with nitric acid, warm, a canary-yellow precipitate shows *phosphate.* (Unless phosphites and hypophosphites have been proved absent, test may be due to these.)

Filtrate from calcium chloride precipitation contains boric acid. Add dilute hydrochloric acid in excess, concentrate. Divide into two portions.

Borate.—Place a few drops on turmeric paper and hang up to dry. A red color, changing to blue with ammonia, indicates *borate.* To the balance of one portion add an

equal volume of concentrated sulphuric acid, cool, add two volumes alcohol and place in a thick-walled test-tube or specimen tube provided with a two-horned stopper carrying (1) a glass tube connected with the gas supply and reaching below the surface of the liquid; and (2) a glass tube drawn to a jet and surrounded by glass tubes of greater diameter, constituting a Bunsen burner. Pass illuminating gas through the tube and light it at the jet. A green flame shows presence of boric acid.

Portion B.—To be tested for sulphide, nitrite, nitrate, silicate, arsenate, using separate portions of the solution.

Sulphide and Nitrite.—Acidify a portion with acetic acid and warm slightly. Note odor and test escaping gases with lead acetate and potassium iodide starch paper. The test for nitrite may be confirmed by acidifying another portion with acetic acid and adding a crystal of ferrous sulphate, a brown ring showing *nitrite.* (Sulphide may be found at this point if hydrogen sulphide were used in removing copper.) Acidify a portion with dilute sulphuric acid. Add an equal volume of concentrated sulphuric acid, pour in gently, freshly prepared solution of ferrous sulphate so that the two drugs do not mix. A brown ring shows *nitrate.* (If nitrite has been found the acidified solution should be boiled before treatment with concentrated sulphuric acid and ferrous sulphate. Other acids interfering with the tests are chlorate, chloride, bromide, iodide, ferro and ferri cyanide, and sulphocyanate,and may be removed by treatment of acidulated solution with zinc and boiling [only necessary if chlorate is present] followed by the addition of silver sulphate in slight excess. Filter and use filtrate for test.)

Silicate.—Acidify a portion of the solution with hydrochloric acid, evaporate to dryness, heat residue gently then treat with dilute hydrochloric acid and wash residue with hot water. An insoluble residue indicates *silicate.* Confirm by bead of microcosmic salt, transparency in sodium carbonate bead, and treatment with hydriodic acid.

Arsenate.—Treat a portion of the solution with magnesia mixture, as long as a precipitate forms, filter and wash precipitate, dissolve in concentrated hydrochloric acid, add a little sulphur dioxide and boil until excess is completely expelled. Pass in hydrogen sulphide and a yellow precipitate indicates *arsenate.*

SECOND PORTION

As explained in the introduction, the second portion of this work describes the methods to be employed in manipulating the various classes of medicinal products in order to effect a separation of their constituents according to the preceding scheme.

These products may be roughly divided into three groups—liquids, solids, semi-solids and oily preparations. Under these groups the classes naturally fall as follows:

Liquids

1. Fluid extracts and plain tinctures.
2. Elixirs, glyceroles, wines, cordials, liquors, bitters, vinegars, and syrups.
3. Emulsions.
4. Liniments.
5. Toothwashes and gargles.

Solids

1. Powdered extracts, solid extracts, and concentrations.
2. Pills, tablets, lozenges, troches, and pastilles.
3. Powders, cachets, hard capsules, and dusting powders.
4. Globules and soft capsules.
5. Granular preparations and artificial mineral-water salts.

Semi-solids and Oily Preparations

1. Pastes, ointments, and emollients.
2. Inhalants.
3. Suppositories, crayons, and bougies.
4. Plasters.

Following this is a chapter devoted to the examination of galenical products for digestive properties.

Fluid Extracts and Plain Tinctures

Little need be said with reference to this class; as a general thing a sample will contain the extractive matter and active principles of but a single drug, and an examination will follow the procedure prescribed for separaing those substances which are soluble in water and alcohol. A preliminary manipulation, if necessary, should follow the lines laid down in the following class which describes the procedure to be observed with liquids in general.

Elixirs, etc.

Divided into two subdivisions, those containing sugar, and those without.

With Sugar	Without Sugar
Elixirs	Glyceroles or Glycerites
Syrups	Liquors
Cordials	Bitters
Wines	Decoctions
	Infusions

Liquid tonics, cough mixtures, headache mixtures will fall under one or the other of the above subdivisions.

Elixirs are aromatic, sweetened, spirituous prepara-

tions of medicinal substances, containing a large percentage of sugar. They may contain almost anything in the category of medicine.

A *cordial* is practically the same as an elixir.

A *syrup* is very much the same as an elixir, but without alcohol.

Medicinal wines are solutions of medicinal substances in wine, usually fortified with alcohol, and often with added sugar. They contain, in general, little else than vegetable principles, or albuminous substances as beef extract, with occasionally iron and antimony.

Glyceroles are solutions of medicinal substances in glycerin. Pepsin, hydriodic acid, hypophosphites, heroin, and some others are often administered in this form.

Liquors or *solutions* are solutions of medicinal substances, sometimes containing alcohol or glycerin, but no sugar. A great many substances, both organic and inorganic, may be present.

Bitters are usually strong alcoholic solutions, containing a small amount of vegetable material.

Vinegars are solutions, usually of organic substances, in dilute acetic acid, often aromatized. Alcohol and sugar will sometimes be present.

Decoctions are solutions of vegetable principles obtained by boiling the drug material with water.

Infusions are virtually the same as decoctions.

Elixirs, Glyceroles, etc.

In the case of products falling under any of the above types, first note the odor and taste carefully, for the

presence of many drugs and other substances can be detected at once by this means.

Next note the reaction of the product on litmus paper. Aromatic spirit of ammonia enters into the composition of some preparations, and acetic, phosphoric, hydriodic, and other acids, are often present.

If there is sufficient sample it is well to distill a portion, test the vapors for ammonia or volatile acids, and examine the distillate for ethyl and methyl alcohol, and formaldehyde. Then evaporate the residual solution in the distilling flask on the steam-bath. Note the consistency of the residue; if much sucrose is present the crystals will be apparent and glycerin in any quantity will be observed at this point. Ignite a portion of this residue and note the quantity of ash. Test its reaction on litmus and on phenolphthalein. The presence of any quantity of inorganic material will be noted. Treat another portion of the residue with absolute alcohol; glycerin will dissolve and sucrose will be left behind.

Now proceed with a systematic examination of the sample in order to detect the various principles. Evaporate the alcohol if present. Separate a small portion of the residue and test for ammonium salts. If the product contains much sugar, continue the evaporation over the steam-bath until very concentrated. Treat residue with hot 95 per cent, or stronger, alcohol, stir thoroughly, cool, and decant alcohol. Repeat several times if necessary. This will separate the vegetable principles from the sucrose, the gummy material, and most of the inorganic material, and the subsequent aqueous solution will be much easier to handle. Reserve the residue for future treatment (*A*). It should be noted

that alcoholic solutions of milk-sugar dissolve some inorganic substances. Evaporate the alcoholic solution. The residue may contain alkaloids and their salts, glucosides, and other vegetable principles, resins, synthetic organic substances, organic acids, glycerin, phenols, some sugars, tannins, coloring matters, some metallic salts of organic acids, and certain inorganic salts. Remove a small quantity of the residue on a glass rod, place on a watch-glass over a white surface, and add a few drops of ferric chloride solution; phenols, salicylic acid, and tannic acid will be indicated if present. Treat the balance with water, warm, and decant. Resin and certain gummy material will not go into solution. If anything remains undissolved, add a small quantity of normal sulphuric acid, but do not continue heating for any length of time. Decant acid solution into about two-thirds of the water solution, and if any precipitate forms at this point, stir and filter, wash precipitate thoroughly, and reserve filtrate and washings. Glycyrrhizin and certain substances in other drugs are precipitated on adding acid to an aqueous solution. If any material remained undissolved by the dilute acid, dissolve it in ether or chloroform, if possible, transfer to separatory funnel, shake out with normal acid, and filter acid solution into the main liquid. Evaporate the ether or chloroform, and examine residue for resin.

Place 1 to 2 c.c. of the acid solution in a test-tube and add a drop or two of Mayer's reagent; a precipitate shows the presence of alkaloids. Treat another portion with Wagner's reagent (iodin in potassium iodide), and note whether a precipitate forms If no precipitate occurs when Mayer's reagent is added, the possibility of

the presence of alkaloids other than the xanthin bases is eliminated. If Wagner's reagent fails to give a precipitate, none of the alkaloids, nor a great number of other plant principles or many synthetics, are present. Now proceed with the separation by immiscible solvents. Shake out successively with petroleum ether, ether, chloroform. Evaporate each shake-out before proceeding with the subsequent solvent, and if anything is removed by a solvent, shake out at least three times with it. The residues should be examined according to the scheme of analysis already elaborated. Make solution slightly ammoniacal, and shake out with petroleum ether, ether-chloroform, and alcohol-chloroform, examining residues as above mentioned. The solution may still contain some organic substances which are not removed by immiscible solvents; certain glucosides, and other principles, curarin, narcein. Glycerin may be tested for in this solution.

The balance of the solution, which was not treated with acid nor shaken out with immiscible solvents, should now be examined. Shake out from acid solution with ether and then with chloroform; add ammonia, and shake out with some solvents. Now test the remaining aqueous solution for sugars, organic acids, and inorganic bases which might be present as salts of organic acids. The residue *A* above should now be examined. Remove a portion and test for sucrose, citrates, tartrates, acetates, albuminous material, hypophosphites, hypochlorites, peroxides, and other substances which may become altered by heat. Then ignite the balance of the residue at a low heat, but obtain an ash as free as possible from carbon. If very black cool and treat

with water, allowing the mixture to digest on the steam-bath. Then evaporate the water and ignite again. Caution is to be observed, as some of the alkali salts are volatile at a high temperature.

Treat the residue with water, filter if necessary, and perform the regular scheme of basic and acid analysis with the filtrate. Any material undissolved by water should be treated with acids, or, if still insoluble, fused with sodium carbonate and potassium carbonate, and the products examined for bases and acids.

Examine a portion of the original material for arsenic by evaporating with a mixture of lime and magnesia water, igniting, and introducing the residue into the Marsh apparatus. Be sure the lime and magnesia are free from arsenic, or decompose with nitric and sulphuric acids.

Solutions containing large quantities of glycerin give up their active principles to immiscible solvents often with some difficulty, but by diluting considerably and shaking out with two or three portions of the solvent more than usually employed, the separation will be complete.

If a liquid preparation is designed for indigestion and stomach troubles, it should be tested for its action on starch and albumin, as described under " Digestives."

Emulsions

Emulsions are liquid preparations containing various substances, some in solution, and some held in suspension by gums, yolk of egg, etc. They are often employed as a means of presenting oily substances and aromatic balsams.

Emulsions may contain acacia, tragacanth, Irish moss, Indian gum, dextrin, quillaja, gelatin, or yolk of egg; sugar is sometimes present, saccharin, salicylic or benzoic acid, a few alkaloids, cod-liver and other oils (petrolatum) and hypophosphites make up the list of the ordinary substances which are liable to be found. Alcohol is seldom met with.

Note the odor, taste, and reaction of the sample.

Before proceeding further, the emulsion should be broken. This may be done by diluting with water in a separatory funnel, and either agitating, heating, cooling with ice-water, adding a little alcohol, and, in rare instances, by lead acetate.

Add 1 to 2 c.c. normal sulphuric acid. Add ether and shake. This will dissolve the oily material. By using considerable of the solvent and adding a little alcohol, if necessary, a separation is not difficult. Draw off ethereal layer and repeat operation twice. Combine the ether solutions, and filter into another separatory funnel. Shake out with a 5 or 10 per cent solution of caustic alkali, which will remove any phenols, creosote, free fatty and other organic acids. Separate, evaporate the ether, and examine the residue for fixed oils and fats.

The identification of fixed oils and fats includes determinations of the iodin number, refractive index, saponification number, and certain special color reactions, such as the Halphen test for cottonseed, the Baudoin and Villavecchia tests for sesame, the sulphuric and nitric acid reaction with cod liver, and the vesicating action of croton oil on the skin of the forearm.

Treat the alkaline solution with a slight excess of acid and shake out with ether. Separate and evaporate the

ether, and examine the residue for phenols, creosote, salicylic or benzoic acid, and fatty acids.

Next examine the aqueous layer containing the gums. Neutralize with ammonia, and evaporate either to dryness over steam-bath, and treat the residue three times with alcohol, or concentrate to small bulk and add considerable alcohol, which will precipitate the gums. If the first procedure is used, evaporate the alcoholic solution obtained, treat the residue with water and a few c.c. of normal sulphuric acid, and then proceed with the treatment with immiscible solvents as described under liquid preparations of the previous class. The portion insoluble in alcohol should be examined for gums and metallic salts. If the second procedure is adopted, filter from the precipitated gum, evaporate the filtrate, treat the residue with water and normal sulphuric acid, and proceed with the treatment with immiscible solvents. Then evaporate and examine residue for metallic salts and salts of organic acids. Then examine the gummy residue on the filter.

The emulsifying agents may consist of acacia, tragacanth, Indian gum, Irish moss, gelatin, and albumin. With the exception of Irish moss they will all be thrown out by alcohol. Acacia is soluble in cold water, gelatin in hot water. Albumin will be rendered more or less insoluble by the precipitation and will be entirely thrown out on boiling. If either of these substances are indicated perform the tests given on page 102 for Proteins and Albumins.

Tragacanth forms a pasty mass with water and Indian gum swells up but does not dissolve.

Prepare a 2 per cent solution of the gum in water,

filtering if necessary. To a portion add a few drops tincture of guaiac, which gives a blue color in presence of acacia. To another portion add copper sulphate followed by sodium hydroxide, which with acacia produces a precipitate which does not dissolve on warming. To another portion add $2\frac{1}{2}$ times its volume of 50 per cent alcohol and a 25 per cent solution of ferric chloride (free from acid); acacia gives a gelatinous precipitate often slow in forming.

Tragacanth has a saponification value of 140–186 and acacia 10–12. The determination of this value is of assistance in identifying the gum present.

Indian gum mucilage on boiling after the addition of a few c.c. of concentrated hydrochloric acid develops a deep pink color. If this gum is suspected, introduce some of the mucilage into a flask, add 2 c.c. syrupy phosphoric acid and digest over the steam-bath. Acetic acid is evolved if Indian gum is present.

Treat 25 c.c. of a mucilage of the gum with an equal portion of 4 per cent borax solution and let stand overnight. Tragacanth yields a mixture which pours without stringing, while Indian gum produces a stringy mixture which often will not pour out of the flask.

Irish moss gives no precipitate with alcohol, borax or lead acetate, but is thrown out by lead subacetate. Quince-seed mucilage gives no precipitate with borax or alcohol, but is precipitated by lead acetate and subacetate.

Liniments

These preparations intended for external use, consist of solutions of camphor, menthol, eucalyptol, thujone,

cantharides, capsicum, turpentine, mustard oil, certain drugs as aconite, belladonna, opium, potassium iodide, iodin, and mercury in a menstruum of alcohol or chloroform; sometimes with ammonia and again in a menstruum of some fixed oil, croton, cotton-seed, sesame, almond, or an alcoholic solution of soap and occasionally glycerin or acetic acid, and often highly flavored with some aromatic oil as sassafras, peppermint, rosemary, or thyme. Products of this type should be examined carefully for methyl alcohol and acetone, as they are sometimes substituted for ethyl alcohol.

Examine first with litmus paper, first holding the moistened paper over the surface of the liquid which is being agitated. NH_3 and any volatile acid is readily detected in this way. Then test the liquid itself with litmus. If the mixture is acid, add a little sodium carbonate and then a small quantity of tannin. If alkaline, neutralize with tannin or with a mineral acid, subsequently treating with sodium carbonate and tannin. Dilute with water, place in a distillation apparatus, and distill until no more volatile oil and solvent come off. Then remove receiver and examine distillate. The volatile oils used can often be detected by their characteristic odors, with which one should have previously become familiar.

To obtain the alcohol in a state of comparative purity treat the distillate with sodium chloride until no more crystals will dissolve, then pour into a separatory funnel, add a few crystals NaCl in excess, and shake out two or three times with low-boiling petroleum ether. This removes the volatile oils and leaves the alcohol behind in the aqueous solution. After separating, distill the aque-

ous layer again and examine the distillate for both methyl and ethyl alcohols and acetone. This solution may still contain camphor, but its presence will not affect the test for alcohol and acetone.

Evaporate the petroleum-ether layer at a low temperature and examine the residue for chloroform.

In testing for non-volatile ingredients a fresh portion of the sample should be used. Evaporate over the steam-bath until no further decrease in the volume takes place. Watch the evaporation, and note whether any vapors of iodin are evolved; also hold a piece of paper moistened with starch solution in the vapors, and in the presence of iodin it will be turned dark blue. When no further diminution takes place, remove a small quantity of the residue, place it in a test-tube, add 1 to 2 c.c. of sodium hydroxide solution, and test for ammonium salts. Remove another small quantity and ash it. The presence of a comparatively large residue indicates that inorganic salts are present.

Now treat the residue with warm water and transfer to a separatory funnel, using ether if much oily material is present. Shake out with ether until all free oil and fats are dissolved; separate the ether layer and reserve for further examination. Should there be no oil or fat, this shaking out with ether may be dispensed with, but the idea of the procedure is to separate any free fats and oils from the fatty acids which will come from the soap if this is present. If any material remained in the evaporating dish, after treatment with water and ether, it should now be treated with dilute sulphuric acid, and the solution added to the liquid in the separatory funnel which has already been shaken out with ether. Note the appear-

ance of any precipitate or turbidity in the aqueous liquid on the addition of the acid solution. Fatty acids from soap will separate at this point. Shake out with ether, evaporate, and examine the residue for fatty acids, capsicum, mustard oil, phenol, cantharides (if these have not been removed in shaking out the fats). Now add ammonia in excess, and shake out successively with ether, chloroform, and chloroform-alcohol 2 : 1. Examine residues for alkaloids, particularly aconite (with care, remembering that the solution under examination is for external use), belladonna, and opium alkaloids. Evaporate off any solvent and excess of ammonia, and examine the solution for glycerin and inorganic salts. If desirable, evaporate a fresh portion of the sample, ignite at a low temperature, and examine the ash. The ethereal solution containing the free fats and oils should now be examined in detail. Shake out first with sodium bicarbonate to remove acids, then with dilute sodium hydroxide, and test this solution for phenols. Then evaporate ether and examine residue for capsicum and cantharides, and identify the fixed oil or fat. The above procedure is general for a liniment containing any or all of the ingredients which might occur. In many cases it can be greatly simplified, as one will determine as the analysis proceeds.

Identification of Volatile Oils

The procedure given was suggested by Nelson.[1]

A liberal sample of the preparation, neutralized if acid or alkaline, is submitted to steam distillation and the undissolved oily layer separated from the distillate.

[1] J. Amer. Pharm. Assn., 6, 1917, 543.

The physical constants of the volatile oil mixture are first determined. The density is taken with a small Sprengel tube. The optical rotation and index of refraction are determined, and the boiling temperature is taken, keeping the fractions separate for each 10° difference and noting the amount and odor of each fraction. This will often afford a clue to the nature of the mixture and perhaps direct attention to some of the components.

Aldehydes (and Some Ketones)

Separation.—The oil (or a suitable fraction) is shaken with an equal volume of a saturated solution of sodium hydrogen sulphite in a separatory funnel and allowed to stand with occasional shaking for from eight to twelve hours. If crystals separate they are filtered off, the aqueous layer is separated and the crystals added. To this solution add sufficient sodium carbonate to neutralize the acid sulphite, and distill with steam. Aldehydes will pass over into the distillate and will usually be recognized by their odor.

Benzaldehyde will indicate oil of bitter almonds; cinnamic aldehyde, oil of cassia; pulegone, oil of pennyroyal; methyl nonylketone, oil of rue; thujone, oils of tansy, wormwood, or sage. (The last three are ketones which react like aldehydes with sodium hydrogen sulphite.)

Phenols: Separation

The oil left in the separatory funnel after treatment with sodium hydrogen sulphite is shaken with two or three times its volume of a 5 per cent solution of potas-

sium hydroxide. After the undissolved oil has separated the aqueous layer is filtered through a wet filter and a slight excess of dilute hydrochloric acid is added. A turbidity at this point will indicate the presence of phenols. Methyl salicylate separates with the phenols.

If the odor indicates the presence of methyl salicylate, take up the separated phenols in a little ether; separate the ether solution and transfer it to a small flask; add from 5 to 10 c.c. of a 5 per cent potassium hydroxide solution and warm on a water-bath under a reflux condenser to saponify the ester. Then pass in carbon dioxide to saturation and extract the phenols (free from methyl salicylate) with ether. Acidify the aqueous solution and extract with ether; if methyl salicylate is present a residue of salicylic acid will be left on evaporating the ether, which can be identified by its melting-point and by the violet color its solutions give when treated with ferric chloride solution.

If methyl salicylate is not present the saponification is omitted. Evaporate the ethereal solution containing phenols at room temperature. The phenols which may be encountered include thymol and carvacrol (from oil of thyme), eugenol (from oil of cloves), and diosphenol (from oil of buchu). Observe whether the separated phenol shows any tendency to crystallize (thymol, diosphenol). Thymol and diosphenol may be separated from the more " acidic " phenols as follows: Dissolve the mixture in 5 per cent potassium hydroxide solution and distill with steam. Thymol and diosphenol will come over from the alkaline solution while ordinary phenol and most of the eugenol will remain in the distilling flask and can be recovered with ether.

Phenols: Identification

Thymol: Crystalline, m.p. 50.5–51.5°. Identify by U. S. P. test (greenish-blue color on adding one drop each of sulphuric and nitric acids to its solution in glacial acetic acid).

Carvacrol: Liquid isomer of thymol, odor like thymol.

Diosphenol: Crystalline, m.p. 83°, peculiar minty odor. With alcoholic ferric chloride its alcoholic solution gives a dark-green color. Its solutions reduce ammoniacal silver nitrate and Fehling's solution.

Eugenol: Liquid, odor of cloves, m.p. of benzoate, 67–70°. Its alcoholic solution gives a blue color with ferric chloride.

Ketones: Separation

The oil remaining after the extraction of aldehydes and phenols is now to be used for the separation of ketones. Advantage is taken of the property which ketones have of combining with semicarbazide to form crystalline, more or less difficulty soluble, and difficultly volatile semicarbazones. From ¼ to 1 gram of semicarbazide hydrochloride and an equal amount of sodium acetate are dissolved in the least possible amount of water. The oil or its fraction (not over 5 c.c.) is added and enough alcohol is stirred in to give a clear solution. (Some NaCl may be precipitated.)

Let the mixture, which should be in a small stoppered flask, stand twelve to twenty-four hours and then dilute with water. If much ketone is present the oil which separates will soon crystallize more or less completely. If crystals separate, filter. In any event separate the

oil, transfer it to a distilling flask, and distill with steam until the volatile oil is removed. If any ketone is present a crop of crystals should now separate from the residue left in the distilling flask if it is cooled and shaken. Filter off the crystals in a Buchner funnel and unite with any that may have separated previous to distillation.

To recover the ketones from their semicarbazones, transfer the semicarbazones to a saponification flask, reserving a portion for melting-point and other determinations. Add from 5 to 10 c.c. of 25 per cent sulphuric acid, stopper the flask, and heat on the steam-bath until the crystals are decomposed. If camphor was present alone or in preponderating amount, it can be seen sublimed into the neck of the saponification flask. Cool and open the flask and note the odor.

Ketones: Identification

Carvone: Liquid, from caraway and spearmint oils, b.p. 230–231°; m.p. of oxime, 72°.

Pulegone: Liquid, from oil of pennyroyal, minty odor, b.p. 222–223°; m.p. of semicarbazone, 168°.

Menthone: Liquid, from peppermint, pennyroyal, and buchu oils, minty odor, b.p. 207–208°; m.p. of semicarbazone 184°.

Camphor: Crystalline, from camphor and rosemary oils, m.p. 175–176°; m.p. of semicarbazone, 236–238°; m.p. of oxime, 118–119°.

Thujone: Liquid, from the oils of thuja, wormwood, tansy and sage, peculiar odor like wormwood, b.p. 200–201°; m.p. of α-thujone semicarbazone, 186–188°; m.p. of β-thujone semicarbazone, 174–175°.

Methyl nonyl-ketone: Liquid, from oil of rue, odor like oil of rue, b.p. 226°, m.p. +13.5°; m.p. of semicarbazone, 123–124°; m.p. of oxime, 46–47°.

Alcohols, Esters, Ethers and Oxides

The volatile oil remaining unacted on by the previous methods of treatment may contain alcohols (as menthol, sabinol, santalol, borneol and terpineol), esters (as menthyl acetate, and bornyl acetate), and phenol ethers (as methyl chavicol, safrol, anethol, and apiol), or oxides (as cineol).

Previous to the further examination of the oil it should be saponified by boiling with an excess of alcoholic potassium hydroxide in order to decompose any esters present. The alcoholic solution is then diluted with sufficient brine to precipitate the oil completely, and the brine solution can be used for the identification of organic acids derived from esters.

There is no good general method for separating the alcohols as a class, and the further examination will therefore be governed by the judgment of the analyst as to what alcohols are likely to be present.

The primary alcohols, such as geraniol, can be separated by the calcium chloride compounds or as acid phthalic esters, provided they are present in sufficient amount (at least 25 per cent of the mixture).

The conversion of alcohols into esters difficultly volatile with steam will be successful in some cases. Thus by heating menthol with benzoic anhydride for two hours at 160–170° menthyl benzoate is formed, and by distilling the mixture with steam the ester, being less volatile,

remains in the distilling flask, is separated, and the menthol recovered by saponifying. The same method is, of course, applicable to any of the more stable alcohols provided they are esterified under these conditions and give benzoates slightly volatile with steam. The identification of the tertiary alcohols is even a more difficult matter, as they are more or less dehydrated on heating with acid anhydrides, but they are not often encountered in a medicinal preparation. When obtained in fairly pure form the alcohols may be characterized by the melting-points of their phenyl urethanes. Sabinol is the alcohol occurring in oil of savin, and since this oil is frequently employed as an abortifacient it should not be overlooked. The best chemical method for identifying sabinol consists in oxidizing it by means of potassium permanganate to α-tanacetogen dicarboxylic acid (m.p. 140°).

Safrol may be found in the higher boiling fractions of the oil, its boiling-point being 233°. The characteristic odor of safrol will serve to direct attention to it, and it can be identified by its oxidation product, a homopiperonylic acid which melts at 127–128°. This is obtained by the oxidation of safrol with potassium permanganate. Another phenol ether which may be encountered in medicinal preparations is apiol. This boils at 294° and will therefore be found in the last fraction of the oil. Apiol has a faint parsley odor. On boiling with alcoholic potassium hydroxide apiol is converted into isoapiol, which melts at 55–56°. Tri-brom apiol melts at 88-89°. Unless present in relatively large amount its identification, on account of its faint odor, is very difficult.

Cineol (b.p. 175°) is separated in the first fractions of

the oil. Its odor, which suggests eucalyptus oil, may direct attention to it if there is not too much interfering material. Cineol is an important constituent of eucalyptus and cajeput oils and is often used in medicine in pure form, being more commonly known as eucalyptol.

It combines with phosphoric or arsenic acid, giving unstable crystalline compounds from which cineol can be recovered by adding warm water. Its iodole compound (m.p. 112°) is characteristic, but rather difficult to prepare from impure cineol.

Sulphur Compounds, Mustard Oils

The esters of isothiocyanic acid, characterized by their penetrating odor, constitute a special group of sulphur compounds.

Volatile mustard oil obtained from black mustard, Brassica nigra, is mainly allylisothiocyanate, and as this boils at 151° it will be found in the first fraction of the oil and will be recognized by its pungent odor.

Tooth Washes and Gargles

These are usually antiseptic solutions, either acid or alkaline in reaction, the acidity being due to boric acid, and the alkalinity to sodium or potassium salts.

In general a gargle is an aqueous or hydroalcoholic solution of boric acid, borax, sodium bicarbonate, sodium benzoate, sodium phosphate, sodium sulphate, potassium chlorate, potassium carbonate, ammonium chloride, containing the oils of gaultheria, eucalyptus or eucalyptol, pinus pumilio, coriander, and often with formaldehyde, hydrogen peroxide, carbolic acid, and thymol.

In the tooth washes the composition will run to soap and glycerin with the above-mentioned flavors, together with the oils of cassia and clove and tincture of myrrh. They will often be colored with cudbear, cochineal, rosolic acid, methyl orange, and salts of berberin. If alcohol is found it should be examined carefully to determine whether it consists wholly or in part of methyl alcohol. First test the solution with litmus paper; note the odor and taste, distinguishing, if possible any of the aromatic constituents and oils used in flavoring. Make special tests for formaldehyde and hydrogen peroxide. Place the solution in a distillation flask, dilute with water, and distill until alcohol is all over. Examine the distillate for alcohol, and make special test for methyl alcohol. If essential oils are present in quantity, they should be removed as described under "Liniments." If formaldehyde is present in the sample, it will come over with the distillate, and must be removed before testing for alcohol. This may be accomplished by adding an excess of metaphenylenediamine hydrochloride, which forms an insoluble precipitate with the formaldehyde. Redistill and examine the distillate for alcohol. Residue in distillation flask divide into two parts. Place one portion in separatory funnel and add dilute sulphuric acid; extract with ether and examine ether residue for benzoic acid, phenol, or other substances which might be removed. If the preparation under examination contains a soap the fatty acids will appear at this point. Then shake out with chloroform and examine residue. Add ammonia in excess and extract successively with ether and chloroform, examining any residue for alkaloids. Then evaporate the residual solu-

tion and examine residue for glycerin. Ignite at a low temperature, and examine ash for inorganic salts. The second portion should be examined for ammonium salts, sulphates, free boric acid, and also the dye present.

Solid Extracts, Powdered Extracts, and Concentrations

These products alone are among the least common of any substances that claim the attention of the drug analyst. They often take part in the preparation of pharmaceuticals, but alone, one is seldom called to analyze them, and when they are sold in this way they are usually labeled so that an identification is not difficult.

They are virtually evaporated fluidextracts of the plants, and can be examined in practically the same way as the liquid. In case it is desired to identify the particular plant principle, the substance should be dissolved in alcohol, and evaporated with water or weak acid (acetic in case the active principle is unstable or suspected to be so), until the alcohol has been driven off, and then the liquid cooled, filtered, and the filtrate shaken out in turn with the various solvents, and examined as described under the schemes for testing for alkaloids, glucosides, and miscellaneous active principles.

Having identified the constituents, a quantitative determination follows according to the nature of the substance found. The Pharmacopœia has set a standard for a number of solid extracts, and assay methods are given under them. In other cases a procedure similar to that adopted for the fluidextract in question may be applied.

Concentrations are usually the principles of various plants, in a more or less purified state. Some of the more common are:

Aletrin (Star-grass; Unicorn Root)
Apocynin (Bitter Root)
Asclepiadin (Pleurisy Root)
Baptisin (Wild Indigo)
Cascarin (Cascara Sagrada)
Caulophyllin (Blue Cohosh)
Cimificugin (Black Cohosh)
Cornin (Dogwood)
Cypripedin (Ladies' Slipper)
Digitalin (Foxglove)
Dioscorein (Wild Yam)
Euonymin (Wahoo)
Gelsemperin (Gelsemium)
Hammamelin (Witch Hazel)
Helonin (Helonias; False Unicorn)
Irisin (Blue Flag)
Juglandin (Butternut)
Leptandrin (Culver's Root)
Lupulin (Humulus Lupulus; Hops)
Phytolaccin (Poke Root)
Podophyllin (Mandrake)
Sanguinarin (Blood Root)
Scutellarin (Scullcap)
Senecin (Life-root)
Viburnin (Cramp-bark)

Pills, Tablets. Lozenges, Troches, Pastils

In the composition of pills and tablets one is liable to find about everything in the realm of pharmaceutical chemistry; new formulas are springing into existence every day, and the number of combinations is legion.

Pills usually have some form of mass as a basis, and in this the medicament is incorporated. The base may contain glucose, honey, soap, syrup, glycerin, tragacanth, vaselin, lycopodium, starch, confections, acacia, mastic, gypsum, kaolin, dextrin, and charcoal. The product after mixing is usually coated, and this coating may consist of sugar, with or without color, gelatin, gold, silver, keratin (in the case of enteric pills intended to go through the stomach unchanged, and dissolve in the intestines).

There are also pills made by a powder process without a mass base, and sometimes called " friable pills."

Tablets include triturates and compressed tablets with or without sugar or chocolate coating, this last often being a salt of iron instead of " chocolate." Triturates are made up with milk sugar as a base. Excipients are often used with compressed tablets, but the material is usually of such a nature that it can be mixed in the dry state, and the shape of the product is obtained by compression.

Lozenges and troches do not have as wide an application as do pills and tablets, hence the number of possible formulas is much smaller. They consist of powders incorporated with sugar and mucilage, sometimes licorice, currant paste, and the like.

Pastils are usually made up with a base consisting entirely of gum, such as acacia. Their use and consequent variety is limited.

In the case of all preparations coming under this class, with the exception of the pastils, first crush the sample in a mortar, noting particularly the odor which will suggest the presence of many substances. Taste some of the powdered sample. Pastils do not crush readily, and should be treated differently. (See page 150.) Moisten a small quantity with water, and note its reaction on litmus paper. Also test with phenolphthalein both before and after warming; bicarbonate will be indicated by giving no color with phenolphthalein until heat is applied. Ash a portion of the powder, and, if there is much residue, inorganic salts are indicated. Test the reaction of the ash with phenolphthalein. Preparations which are neutral or acid before ignition, and alkaline afterward, contain alkali salts, or plant material. Examine the powder under the microscope; many plant substances can be

identified in this way. It may be necessary to get rid of some of the other material by washing with water or floating in a solution of zinc sulphate or Mayer's reagent. Treat some of the powder in a dry test-tube with a few drops of concentrated sulphuric acid. Note any effervescence in the cold, also the odor given off, and test the gases with lime-water, lead acetate paper, starch-paper, etc. If no action occurs in the cold, warm gently, and note the result. Charring will generally occur on heating, owing to the prevalence of sugar. Test powder for ammonium salts. Test powder for arsenic.

Triturate the ground material from 6–12 or more of the pills or tablets with 95 per cent or stronger alcohol. Filter the menstruum and repeat twice. Preserve any undissolved material for future treatment. Evaporate the alcoholic solution. Note the quantity and appearance of the residue. Test a small portion with ferric chloride, and note the color; tannins, salicylates, phenol derivatives, may be indicated here. Treat the balance with water and warm gently; decant if not completely soluble, treat the residue with normal sulphuric acid, and again warm. If the substance is still unacted upon, treat with ether or chloroform, place in a separatory funnel, and shake out with normal sulphuric acid, adding acid extract to about two-thirds of the other aqueous liquid. Note any precipitate formed on the addition of sulphuric acid; licorice is often present, and the glycyrrhizic acid will precipitate at this point. Remove a small portion of the solution and test with Mayer's and Wagner's reagents; alkaloids are indicated if the former produces a precipitate. If no precipitate is obtained with either of the above reagents, the possibility of the pres-

ence of a large number of organic substances is eliminated. Proceed now with the shaking-out process with immiscible solvents, evaporating and examining each extract in turn before proceeding with the subsequent solvent. When the final shaking out is completed, evaporate the solution to drive off the excess of solvents and ammonia. The residual solution should be examined for organic acids, certain substances which are known to be left behind by immiscible solvents, as glycerin, sugars, and metals which might be present as salts of organic acids.

The portion of the ground sample insoluble in alcohol should be examined for sugars, starch, albumin, organic salts, and gums. Treat with water, and proceed with the aqueous solution according to the scheme of basic inorganic analysis.

The above procedure is recommended as it gives one an insight into the actual composition of the product better than by ignition and subsequent examination of an aqueous or acid solution of the residue. On igniting certain substances their composition is changed to such an extent that the form in which they originally existed is lost. However, it is well to make an ignition of the preparation, and run through an analysis of the ash both as confirmatory, and possibly for detecting substances which may have been overlooked. In many instances it may be necessary to adopt special schemes for the particular preparation under examination, and experience will demonstrate when such a measure is necessary.

If the product is claimed to have digestive properties determine its action on egg albumin and on starch solution; details of which procedure are elaborated under "Digestives."

Pastils

Dissolve the sample in as small a quantity of water as possible. Note odor and reaction to test-papers and solutions. Test a portion for ammonium salts. Add a small amount of normal sulphuric acid, then pour the solution into a considerable excess of alcohol, from five to ten times the amount of the aqueous solution, allow the mixture to stand until the precipitated gums have settled out and then filter. Evaporate the alcoholic solution after neutralizing with ammonia. Examine the residue the same as powdered pill or tablet.

The portion precipitated by alcohol should be examined as described under the portion of the powdered pill or tablet which was insoluble in alcohol. Gums should be examined as described under " Emulsions."

Powders, Cachets, Hard Capsules and Dusting Powders

Powders in general may be composed of a great variety of substances, but an individual powder is generally of simple composition.

A cachet is a powder offered in a protective coating, e.g., conseals.

Hard capsules contain a variety of substances, but the contents are easily removed and may be examined the same as other powders. Hard capsules will often contain solid extracts, which can be removed and then examined as described under Solid Extracts.

Dusting powders will contain only a limited variety of material. They may contain talc, boric acid, salicylic

acid, zinc oxide, chloretone, lycopodium, and starch, flavored with violet, rose, orris, etc.

Tooth powders will contain chalk and powdered soap.

In general these products may be examined by the same procedure recommended for pills and tablets.

Globules and Soft Capsules

These products usually consist of a liquid, sometimes with a solid in suspension enclosed in an air-tight gelatin covering.

Soft capsules are made with flexible gelatin, and are of different sizes. Globules are usually of one size and the gelatin is firmer.

Some of the more important therapeutic agents administered in the form of capsules and globules are castor oil, cod-liver oil, copaiba, creosote, santalwood oil, cassia oil, turpentine, chaulmoogra oil, methyl salicylate, apiol, methylene blue, salol, oleoresin of cubeb, etc.

The individual formulas are not very complex, and nearly all of the ingredients are indicated at once by some physical characteristic. Copaiba, santalwood oil, cassia oil, methyl salicylate and creosote, are readily detected by their odor, and the deep blue color of methylene blue is unmistakable.

The contents should be removed and examined according to the schemes described under the respective headings for a liquid, a solid, or an oily material.

Pills or tablets in suspension can be separated from the oils by treating the mixture with ether.

In case the analyst experiences difficulty when work-

ing with a product containing a large quantity of a volatile oil, the latter may be separated by steam distillation.

Effervescent Preparations and Artificial Mineral Water Salts

Effervescent preparations nearly always contain sodium bicarbonate, tartaric acid, sugar, and the medicinal ingredients. In case the product is in granular form citric acid will also be present.

The medicinal ingredients are limited, and are in such a form as to be readily soluble in water. Remedies for headache are often exhibited in this form, and lithium compounds, magnesium salts, and salicylates, are commonly found.

Artificial mineral water salts consist of inorganic salt mixtures, in which the sulphates, chlorides, bicarbonates and carbonates of the alkalies and magnesium predominate. Formulas of the composition of some of the most prominent on the market are given in Merck's Index, page 385.

An aqueous solution of an effervescent preparation should be acidulated with normal sulphuric acid, and some of the solution tested with Mayer's and Wagner's reagents to detect alkaloids and other organic substances. Then shake out with immiscible solvents from both acid and ammoniacal solution, examining each residue according to the regular scheme. The residual solution should now be evaporated, and after the excess of solvents and ammonia are removed, the residue should be examined for organic acids and metallic salts. Examine for pepsin and other digestives.

An artificial mineral water salt should be examined by following the regular schemes for basis and acid inorganic analysis.

Pastes, Ointments, and Emollients

Pastes and creams may or may not contain an oil or fatty material, and if ingredients of that nature are present, the product is virtually an ointment, and the method of procedure would be the same as for the latter. The semi-fluid nature of pastes may be due to glycerin or to some nitrogenous substance, such as moist casein. Tooth pastes contain a considerable quantity of calcium carbonate, and sometimes calcium phosphate, soap, occasionally pumice, essential oils, and coloring matter.

Creams made up with a casein base will usually be found to contain zinc oxide, coloring matter, essential oils, and salicylic acid or similar preservative.

Emollients are made up sometimes with a base of glycerin, and again with mucilage of Irish moss or the like, and will contain no fixed oil or fat. Starch and boric acid are usually present.

Ointments consist of a base of petrolatum or some fixed oil or fat, often with inorganic substances in suspension, sometimes alkaloidal bodies dissolved as oleates in suspension, camphor, aromatic substances, synthetics, and various other organic bodies. Coloring and flavoring agents are often present. The composition may be as variable as the liquid products. The presence of an oil or a fat is usually apparent from a very cursory examination of the sample. If there is any doubt, treat a small

portion with water and warm, when any fixed oil or fat will melt and separate out on the surface. Note the odor. If neither oil nor fat is present, treat with warm water until nothing further dissolves. If starch or gums are present, it may be necessary to break up the emulsion with alcohol, then filter again, and evaporate off the alcohol. Reserve the residue for future examination and proceed as follows with the solution:

Note the reaction to litmus; to a portion add dilute sulphuric acid and note any precipitate; if soap is present the fatty acids will separate at this point. Shake out with immiscible solvents, and examine the residues for fatty acids and other organic substances, though very few of the latter are liable to be met with. The solution should now be evaporated until free from solvents and ammonia, and examined for inorganic material and organic substances, glycerin, gums, etc., not removed by immiscible solvents; or the portion of the solution which was not acidified in the first place may be used. The material insoluble in water should now be examined for those organic substances which do not dissolve in water, and also for inorganic material. It is well to dry it first, and then treat with alcohol, which will dissolve out most of the organic substances except starch and gums.

Ointments and pastes with oils or fatty bases must be examined somewhat differently: Note the odor; transfer to an Erlenmeyer flask and cover with ether. Shake until all the fatty material, oils, waxes and the like have gone into solution. Filter the ether solution through a creased filter. Repeat if necessary until all the fatty material has dissolved, using a glass rod to break up

resistant waxes. Wash the residue on the filter paper with ether until it is free from grease, and set it aside for future examination. Transfer the ethereal solution to a separatory funnel and shake out with dilute sulphuric acid. The acid will remove organic substances of a basic nature, e.g., alkaloids, if they had been present in the free state or as oleates. To a small portion of the acid solution freed from any adhering ether by warming, add Mayer's reagent and also Wagner's reagent, and note any precipitate. If alkaloids or other organic substances are indicated, render the balance of the solution alkaline with ammonia, shake out with immiscible solvents, and examine residue so as to identify the substances present. Then shake out the ethereal solution with sodium bicarbonate and then with 10 per cent sodium hydroxide. The alkalies will remove the free fatty acids, other organic acids, certain dyes, acid resins, phenols, etc. Separate the alkaline solutions, acidify, and shake out with ether. Filter and evaporate the ether solution which will leave the dissolved substances in such a form that they can be separated and identified. The ether solution may now contain hydrocarbons, paraffin, cerasin, petrolatum; fixed oils, fats and waxes, turpentine, camphor, menthol, some of the higher alcohols, neutral resins, etc. Evaporate carefully to prevent loss of volatile constituents. Examine the residue to identify any fixed oil or fat. Alcohol will separate the turpentine, camphor, menthol, etc., and saponification of the residue and examination of the fatty acids separated by acid and shaken out with ether will aid in identifying the oils, while the unsaponifiable residue will contain the inert hydrocarbons.

The residue on the filter which was insoluble in ether should now be examined. Treat with hot water, filtering if any material remains undissolved. Divide the solution into two portions, reserving one for any special tests that may be necessary. Treat the other portion with immiscible solvents in order to detect alkaloids, glucosides, synthetics, and other organic substances possibly present. Then examine the residue for metallic salts. If any residue was left from the treatment with water, it should be dissolved in acid if possible and the solution examined for metallic salts insoluble in water. If any material remains undissolved by acids, examine it for substances known to be left by that treatment.

Inhalants

These preparations are usually made up with an oily base, though specimens will be found in which no oil is present, the lubricating medium being glycerin. Those of the latter type may be examined according to the general scheme given under Liquids.

The oily type have as a base liquid petrolatum, and sometimes other oils such as sweet almond, olive, and the like; copaiba, oil of tar, oil of eucalyptus and eucalyptol, carbolic acid, Tolu, Peru, guaiacol, creosote, tincture of iodin, iodoform, camphor, thymol, cocain, adrenalin, chloretone, acetozone, ether, and alcohol may all be suspected.

The procedure of analysis should be the same as under Ointments.

Suppositories, Crayons, Bougies

Suppositories are made up in either a base of cacao butter (oil of theobroma), or glycerin mixed with sodium stearate; soap is used and wax and spermaceti are sometimes mixed to stiffen the base.

The medicinal ingredients vary according to the use. Rectal suppositories used for pile remedies often contain opium, stramonium, tannic acid and lead acetate. Iodoform, morphin, belladonna, carbolic acid, and other antiseptics will be found, the latter especially in vaginal suppositories and bougies which are used in gonorrheal affections. Vaginal suppositories will also consist of boric acid, thymol di-iodide, acetanilid, glycerin, ichthyol, iodin, quinin bisulphate, golden seal alkaloids (hydrastin, etc.), chloretone, certain salts of zinc, salts of metals with organic acids as nucleinic, and the like.

Bougies which are used in the urethra will contain gelatin and some gums, but in other respects they are essentially of the same general composition as the other suppositories.

An examination should follow the general lines given under Pastes and Ointments.

Plasters

These products are intended to be adhesive at the temperature of the human body. The base may consist of rubber, Burgundy pitch, gum olibanum, galbanum, rosin, Canada balsam and other resins and gums, wax, soap, lead oleate, etc. A preliminary examination will usually give one an idea as to which is present.

The medicament may consist of aconite, belladonna, opium, arnica, capsicum, ginger, phytolacca, cantharides, camphor, asafetida, ammoniac, mercury, iron, lead oleate, etc.

Place the sample in a beaker and cover with ether. If it does not dissolve readily in this solvent, replace with chloroform, and soak until nothing further will go into solution. Filter into a separator. The insoluble material may consist of soap, inorganic and organic salts, diluent, inert plant constituents, and the cloth on which the plaster was spread.

Dry the insoluble residue and treat with water. Filter, and if anything remains undissolved examine it for starch, metals and metallic salts insoluble in water. Transfer the aqueous solution to a separator, and add normal sulphuric acid, noting any separation of fatty acids due to soap. Extract with immiscible solvents, then make alkaline with ammonia, continuing the extraction with immiscible solvents, and examine carefully the residue left on evaporation. Finally test for the presence of metallic salts soluble in water.

The ether or chloroform solution originally obtained should now be investigated. Add dilute sulphuric acid to the separatory funnel and shake thoroughly. Lead will become apparent at this point, due to the separation of lead sulphate. Draw off the aqueous layer, and continue the addition and extraction with acid until no more separation of lead results. Reserve the ethereal or chloroformic solution. Filter the combined acid extracts, and examine the insoluble substances for lead. To a small portion of the filtered liquid, previously warmed to expel any adhering solvent and then cooled, add a drop of

Mayer's reagent, and the presence of an alkaloid will be indicated by the characteristic precipitate. If no precipitate occurs, add Wagner's reagent. If no precipitate is obtained with either of these reagents, there is little need of testing further for alkaloids. If, however, the latter are indicated, add ammonia to the balance of the solution and shake out with immiscible solvents, examining the residues to determine the particular substance present.

Next shake out the solvent solution with 10 per cent sodium hydroxide, two or three times. Combine the alkaline extractions, acidify with sulphuric acid, shake out with immiscible solvents, and examine residues. Oleic acid from lead oleate will appear at this point; also resin acids, phenols and other substances having acid properties.

Then evaporate the ethereal solution and examine the residue for neutral principles.

Chewing Gums

Chewing gum consists of a base of chicle or cauchillo gum, or of a chicle substitute containing low-grade rubber, resinous constituents of crude rubber, gutta percha or balata, the resene portions of other resins such as dammar and vegetable wax or paraffin.

The other components of a finished gum may be glucose, caramel, sugar, and flavor. Starch is often present in small quantity. Pepsin is often claimed as a medicament and some product designed to break up the tobacco habit will contain strychnin or some other bitter principle.

Cut up the gum in small pieces and transfer to a stoppered flask, cover with chloroform and shake until the resinous ingredients have dissolved. Filter, wash insoluble portion with chloroform and then dry it with a current of air. Digest with a small quantity of cold water, filter and test filtrate for sugar, digestives and alkaloids.

To test for pepsin a portion of the filtrate made slightly acid with diluted hydrochloric acid is added to a bottle containing a weighed amount of egg albumin and a pepsin test conducted as described under " Digestives."

To test for alkaloids treat a portion of the aqueous solution with ammonia, and shake out with chloroform, separate, evaporate solvent, and make appropriate tests on the residue.

The chloroform solution contains the gum base and may hold alkaloids in solution and it should be shaken out with a little normal sulphuric acid, the acid separated, treated with ammonia and shaken out with chloroform. On evaporating the solvent the residue may be subjected to appropriate tests for strychnin and other alkaloids.

Digestives

Preparations intended to relieve stomach troubles and indigestion should be specially examined in order to determine their action on starch and egg albumin, though the rest of the analysis may follow the general procedure outlined for the particular class of products under investigation.

In order to test its action on egg albumin about 5 to 10 grams of the sample, if it is a solid, are ground in a mor-

tar, 10 c.c. dilute hydrochloric acid (9 c.c. dilute HCl+ 291 c.c. H_2O) added, well incorporated with the powder with the pestle, and filtered, this procedure being repeated until the filtrate measures 50 c.c. If the sample is a liquid it can be added directly to the egg albumin. The balance of the test should follow the directions given in the Pharmacopœia for the determination of pepsin, and a blank test performed at the same time for comparison.

To determine whether or not the sample has any action on starch, it is first necessary to demonstrate the presence or absence of substances reducing Fehling's solution; if absent, the procedure is much simplified, as one needs but prove that the preparation has the power to change starch into reducing sugar. If reducing substances occur naturally, a quantitative determination must be carried out, in one case with a known amount of the sample, and in another after the same quantity has been applied to a starch solution. To perform the starch test about 20 grams of neutral potato starch are suspended in 30 c.c. cold water, and after being well mixed the mixture is poured into about 900 c.c. of boiling distilled water, the whole well stirred and boiled for about ten minutes until a homogeneous jelly is obtained, and then cooled rapidly to 40° C. Now provide a number of cylindrical glass tubes which will hold about 100 grams of starch paste, nearly immerse these in a water-bath heated to 40°, and allow to stand until the contents have attained this temperature.

The product which is to be examined for its action on starch should be treated with water, and all acid or alkali avoided. If it is in the liquid form, it may be added directly to the starch paste in the tubes. The tube is

closed with a rubber stopper and shaken vigorously. It is then returned to the water-bath and digested for ten minutes, the tube being shaken from time to time.

At the end of ten minutes' digestion fill a medicine dropper with the digested solution and drop ten drops in a tube containing dilute iodin solution. Agitate and note the color. If blue due to undigested starch continue digestion for a longer period, also add increasing quantities of the samples until it has been demonstrated whether or not any starch-digesting ferment is present.

Scheme for the Rapid Detection of Inhibited Drugs

If the product is a liquid, on distillation chloroform and a trace of acetanilid will be obtained.

Chloroform will be recognized by its settling out as a heavy liquid at the bottom of the flask unless there is a large excess of alcohol. The water should be decanted, and an isonitrile test performed: A small quantity of strong potash solution is added, the mixture warmed and a drop of anilin added, when in the presence of chloroform, the disagreeable odor of phenyl isocyanide will be noted. In case a trace of acetanilid distilled over with the chloroform originally, the disagreeable odor will be apparent at once on warming with potash. However, as a matter of fact, chloroform and acetanilid will seldom, if ever, be found in the same preparations.

The solution, after distillation, or if the original product was a solid, a solution made from it, is rendered slightly acid with dilute sulphuric acid, and then placed in a separatory funnel and shaken with ether three times.

The ether solutions are separated and evaporated and the residue may contain:

Acetanilid, m.pt	110–113°
Acetphenetidin, m.pt	135°
Hydrated chloral	Liquid

Place a watch-glass over the beaker or dish in which the evaporation was made and place over the steam-bath, noting any sublimate. Acetanilid readily sublimes, and the sublimate may be tested for the isonitrile reaction with chloroform and potash.

A portion of the residue is warmed with dilute sulphuric acid over the steam-bath, continuing the evaporation until the volume has diminished about one-half. Cool the liquid, and add a few drops of potassium bromide-bromate reagent. In the presence of acetanilid a yellowish-white precipitate will appear, and in the presence of acetphenetidin a blue color. This test will detect both when they occur together. (The bromide-bromate reagent is made by adding bromin in slight excess to a concentrated aqueous solution of potash, diluting to dissolve any separated salts, and boiling to expel any excess of bromin.)

To test for hydrated chloral treat the residue with a small amount of water, add a few drops of ammoniacal silver nitrate and warm, when a reduction indicates chloral. Warm a second portion of the aqueous solution with Fehling's solution, which will be reduced by chloral.

Hydrated chloral will also give the isonitrile reaction when tested by the same procedure as in the case of chloroform.

In case both chloral and acetanilid were present in the same mixture, one would obtain the isonitrile reaction at once on adding alkali.

Now shake out the solution three times with chloroform in order to remove any of the above substances remaining behind in the solution, and others which will be removed in the presence of acid.

Add dilute potash until the solution is alkaline to litmus, and then shake out three times with petroleum ether. The following substances will be removed:

Cocain—crystals m.pt. 98°;

Beta-Eucain—oil;

Alpha-Eucain—m.pt. 104–105° (very seldom found).

Remove a portion of the residue on the end of the finger and rub it gently over the tip of the tongue; in the presence of any of the above substances a numbness will soon develop, persisting for some time in case the amount is large.

Dissolve the residue in petroleum ether, and pour a small quantity into an evaporating dish. Evaporate the solvent, treat residue with 1 c.c. concentrated nitric acid, and evaporate to dryness over the steam-bath; while residue is still warm add a few drops of N/1 alcoholic alkali and note whether there is any odor of ethyl-benzoate. Cocain will give this pleasant-smelling substance, while neither of the eucains will. Run a comparative test until familiar with the odor.

Evaporate a small portion of the ethereal solution on a microscope slide, treat with very dilute sulphuric acid, and add a drop of gold chloride solution, noting the appearance of the crystals formed under the microscope.

Perform this latter test, using platinum chloride solution and palladium chloride solution; both reagents give characteristic crystals with the above alkaloids.

Now shake out with sulphuric ether, which will remove the following substances:

Codein (methyl morphin) m.pt. 152–159°;
Dionin (ethyl morphin) m.pt. of free base, 89–90°;
Heroin (diacetyl morphin) m.pt. of free base, 171°;
Apomorphin;
Peronin (Benzylmorphin).

Separate the residue obtained into a number of fractions in small porcelain evaporating dishes, and perform tests with color-producing reagents as indicated on chart accompanying page 78.

Codein differs from dionin by the fact that the free base is more readily soluble in ammonia.

Heroin on treatment with alcohol and sulphuric acid gives the odor of ethyl acetate.

Codein and heroin are the only two products in this fraction which will be met with to any extent.

Now shake out the solution three times with chloroform and discard the chloroform. Then shake out the alkaline liquid three times with a mixture of chloroform and alcohol 2 to 1. Separate and evaporate the solvent and the residue may contain:

Morphin, m.pt. 254° on rapid heating.

Test with color-producing reagents as indicated on chart accompanying page 78.

Reagents

The solutions have been made to conform as nearly as practicable with those given in the Pharmacopœia and in most cases directions for preparation are given on the basis of 100 c.c. quantities.

Whenever the word "water" is used it is understood to mean "distilled water."

Acid, Acetic, Glacial

Acid, Acetic.....36 per cent.-35 c.c. glacial acid with 65 c.c. water.

Acid, Acetic Dilute 10 per cent...6 c.c. glacial with 94 c.c. water.

Acid, Hydrochloric Conc.

Acid, Hydrochloric Dilute, 10 per cent.....30 c.c. hydrochloric acid conc. with 70 c.c. water.

Acid, Nitric Conc.

Acid, Nitric Dilute, 10 per cent..11 c.c. nitric acid conc. with 89 c.c. water.

Acid, Sulphuric Conc.

Acid, Sulphuric Dilute, 10 per cent.....7 cc. sulphuric acid conc. with 93 c.c. water.

Alcohol, 95 per cent.

Ammonia Water (Stronger), 28 per cent.

Ammonia Water Dilute, 10 per cent.....36 c.c. stronger ammonia water with 64 c.c. water.

Ammonium Carbonate.....20 grams ammonium carbonate U. S. P. dissolved in 20 c.c. ammonia water, 10 per cent, and 80 c.c. water.

Ammonium Molybdate.....10 grams molybdic acid dissolved in 42 c.c. ammonia water 10 per cent, and poured into a mixture of 63 c.c. water and 63 c.c. nitric acid conc.

Ammonium Oxalate.....4 grams dissolved in 100 c.c. water.

Ammonium Sulphate.....10 grams dissolved in 100 c.c. water.

Ammonium Sulphide.....6 c.c. ammonia water 10 per cent are saturated with hydrogen sulphide and then diluted with 40 c.c. ammonia water 10 per cent. To prepare the yellow ammonium sulphide add 1 to 2 grams of sulphur and shake until dissolved.

Ammonium Vanadate (Mandelin's Reagent).....1 gram dissolved in 100 c.c. sulphuric acid conc.

Barium Chloride.....10 grams dissolved in 100 c.c. water.

Barium Hydroxide .....Saturated solution.

Bromin Water.....3 c.c. dissolved in 100 c.c. water. Freshly prepared.

Cadium and Potassium Iodide....5 grams of equal parts by weight of the two salts dissolved in 100 c.c. water.

Cadmium Chloride.....10 grams dissolved in 100 c.c. water.

Calcium Chloride .....10 grams dissolved in 100 c.c. water.

Calcium Hydroxide.....Saturated solution.

Calcium Hypochlorite.....10 grams triturated with 20 c.c. water, filtrated and repeated and the filtrate made up to 100 c.c.

Calcium Sulphate.....Saturated solution.

Chlorine Water.....0.5 gram potassium chlorate treated with 2 c.c. hydrochloric acid conc. in a flask fitted with a perforated stopper, warmed on steam-bath and when the flask is full of gas add 100 c.c. water.

Cobalt Nitrate.....10 grams dissolved in 100 c.c. water.

Cobaltous Chloride.....2 grams dissolved in 100 c.c. water and 1 c.c. hydrochloric acid.

Copper Acetate.....1 gram dissolved in 1000 c.c. water. If solution becomes cloudy add few drops acetic acid until clear.

Copper Ammonium Sulphate....To be freshly made. To a solution of copper sulphate add ammonia until precipitate first formed is not quite dissolved.

Copper Sulphate.....10 grams dissolved in 100 c.c. water.

Fehling's Solution.....1. 7 grams copper sulphate dissolved in 100 c.c. water.

2. 35 grams Rochelle salt and 10 grams sodium hydroxide dissolved in 100 c.c. water.

Formaldehyde-Sulphuric Acid (Marquis Reagent).....10 c.c. formaldehyde solution in 50 c.c. sulphuric acid.

Fuchsin-Sulphurous Acid.....0.5 gram fuchsin and 9 grams sodium bisulphite dissolved in 500 c.c. water and treated wi h 10 c.c. hydrochloric acid.

Gold Chloride.....3 grams dissolved in 100 c.c. water.

Iodin (Wagner's Reagent).....2 grams with 6 grams potassium iodide dissolved in 100 c.c. water.

Iron Chloride (Ferric).....10 grams dissolved in 100 c.c. of recently boiled water.

Iron Sulphate (Ferrous).....To be freshly made. 1 gram dissolved in 10 c.c. of recently boiled water.

Lead Acetate.....10 grams dissolved in 100 c.c. water.

Lead Acetate, Alcoholic.....3 grams of crystals dissolved in 100 c.c. alcohol.

Lead Subacetate.....18 grams lead acetate dissolved in 70 c.c. water, added to 11 grams of lead oxide (Litharge, PbO) in a porcelain dish, boiled for one-half hour, filtered and made up to 100 c.c.

Magnesia Mixture..... 10 grams magnesium sulphate and 20 grams ammonium chloride dissolved in 80 c.c. water and 42 c.c. ammonia water 10 per cent added.

Magnesium Sulphate.....10 grams dissolved in 100 c.c. water.

Mercuric Chloride.....5 grams dissolved in 100 c.c. water.

Mercuric Chloride, Alcoholic.....6 grams dissolved in 100 c.c. alcohol 95 per cent.

Mercuric Nitrate.....40 grams red mercuric oxide dissolved in 45 grams of nitric acid (conc.) and 15 c.c. water.

Mercuric-Potassium Iodide
(Mayer's Reagent).....1.3 grams mercuric chloride dissolved in 60 c.c. water added to 5 grams potassium iodide dissolved in 10 c.c. water and made up to 100 c.c.

Mercurous Nitrate.....10 grams in 100 c.c. water. Keep over metallic mercury.

Millon's Reagent.....10 grams mercury dissolved in 10 grams nitric acid (conc.) with aid of heat, and then diluted with two volumes of water.

Oxalic Acid.....5 grams dissolved in 100 c.c. water.

Palladous Chloride.....5 grams dissolved in 100 c.c. water.

Phenolphthalein.....1 gram dissolved in 50 c.c. alcohol and 50 c.c. water added.

Phosphomolybdic Acid.
(Sonnenschein's Reagent).....Prepare ammonium phosphomolybdate and after washing with water, boil with nitric acid and expel ammonia, evaporate to dryness and dissolve in 10 per cent nitric acid.

Phosphotungstic Acid.
(Scheibler's Reagent).....20 grams sodium tungstate and 15 grams sodium phosphate dissolved in 100 c.c. water containing a little nitric acid.

Picric Acid (Hager's Reagent)....1 gram dissolved in 100 c.c. water.

Platinic Chloride.....13 grams dissolved in 100 c.c. water.

Potassium Bromide-Bromate.....To a concentrated solution of potassium hydroxide add bromin to saturation, boil off excess and dilute with an equal volume of water.

Potassium-Cadmium Iodide
(Marme's Reagent).....2 grams cadmium iodide added to a boiling solution of 4 grams potassium iodide in 12 c.c. water and mixed with an equal volume of saturated solution potassium iodide.

Potassium Carbonate.....10 grams recently dehydrated at 130° C., dissolved in 100 c.c. water.

Potassium Chromate.....10 grams dissolved in 100 c.c. water.

Potassium Cyanide.....To be freshly prepared. 1 gram dissolved in 10 c.c. water.
Potassium Dichromate.....10 grams dissolved in 100 c.c. water.
Potassium Ferricyanide.....10 grams dissolved in 100 c.c. water, freshly made.
Potassium Ferrocyanide.....10 grams dissolved in 100 c.c. water.
Potassium Hydroxide.....6 grams dissolved in 94 c.c. water.
Potassium Iodide.....20 grams dissolved in 100 c.c. water.
Potassium Permanganate.....0.5 gram dissolved in 100 c.c. water.
Potassium Sulphate.....1 gram dissolved in 100 c.c. water.
Potassium Sulphocyanide.....1 gram dissolved in 100 c.c. water.
Pyrogallol, Alkaline.....To be freshly made as wanted.
Resorcinol.....1 gram dissolved in 100 c.c. water.
Silver nitrate.....5 grams dissolved in 100 c.c. water.
Silver Nitrate, Ammoniacal.....5 grams silver nitrate dissolved in 100 c.c. water and treated with ammonia water 10 per cent until precipitate is not quite redissolved.
Silver Sulphate.....1 gram treated with 100 c.c. of water. To be filtered as used.
Sodium Acetate.....10 grams dissolved in 100 c.c. water.
Sodium Bisulphite.....To be freshly made. 30 grams dissolved in 100 c.c. water. If sulphur dioxide odor is strong add 20 per cent sodium hydroxide until scarcely noticeable.
Sodium Bitartrate.....3.5 grams tartaric acid boiled with 80 c.c. water, sodium carbonate added until neutral and then 3.5 grams tartaric acid added and solution made up to 100 c.c.
Sodium Carbonate.....10 grams dissolved in 100 c.c. water.
Sodium-Cobaltic Nitrite.....4 grams cobalt nitrate and 10 grams sodium nitrite dissolved in 50 c.c. water, 2 c.c. acetic acid 36 per cent added and then water to 100 c.c.
Sodium Cyanide.....To be freshly prepared. 1 gram dissolved in 10 c.c. water.
Sodium Hydroxide.....6 grams dissolved in 94 c.c. water.
Sodium Hypobromite.....1 c.c. bromin dissolved in 15 c.c. water containing 4 grams sodium

hydroxide, then diluted to 20 c.c. To be freshly prepared.

Sodium Hypochlorite.....9 grams calcium hypochlorite triturated with 20 c.c. water, filtered and repeated, and washed with 10 c.c. water, filtrate mixed with 6.5 grams sodium carbonate monohydrated dissolved in 30 c.c. water, filtered, washed and made up to 100 c.c. Freshly prepared.

Sodium Nitroprusside.....1 gram dissolved in 10 c.c. water. Freshly prepared.

Sodium Phosphate.....10 grams dissolved in 100 c.c. water.

Sodium and Potassium Tartrate (Rochelle Salt) .....10 grams dissolved in 100 c.c. water.

Sodium Sulphide.....10 grams dissolved in 100 c.c. water.

Sodium Tartrate.....10 grams dissolved in 100 c.c. water,

Sodium Thiosulphate.....2.5 grams dissolved in 100 c.c. water.

Stannous Chloride.....Pure tin boiled with hydrochloric acid (conc.) having metal in excess; when saturated, crystals will form, which are separated and drained and dissolved in 10 parts water and the solution preserved in a well-stoppered bottle containing tin foil.

Starch.....0.5 gram starch mixed with 10 c.c. water and added to 90 c.c. boiling water.

Sulphomolybdic Acid (Froehde's Reagent)..... 10 grams molybdic acid or sodium molybdate dissolved in 100 c.c. sulphuric acid conc.

Tannic Acid..... ..10 grams dissolved in 10 c.c. alcohol and 90 c.c. water added.

Tartaric Acid.....10 grams dissolved in 30 c.c. water.

Turmeric.....Powder is digested with several portions of water which are discarded. Then treat with six times its weight of alcohol for several days and filter.

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